		cell line, which is a suspension	cancers, such as, leukemia,
		culture of leukemia cells that	lymphoma, melanoma, glioma
		produce IL-2 when stimulated.	(e.g., malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
	-		disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,
			meningitis, Lyme Disease,
			cardiac reperfusion injury, and

					asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HT HT	НОЕВК34	1359	Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immuno cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the activation of monocytes and T cells. Such assays that may be used or routinely modified to	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammation and inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications

diffferentiation activity of	(e.g., rheumatoid arthritis,
polypeptides of the invention	systemic lupus erythematosis,
(including antibodies and	multiple sclerosis and/or as
agonists or antagonists of the	described below) and
invention) include assays	immunodeficiencies (e.g., as
disclosed in Miraglia et al., J	described below). Preferred
Biomolecular Screening 4:193-	indications also include
204(1999); Rowland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
158:2919-2925 (1997), the	disease, inflammatory bowel
contents of each of which are	disease, sepsis, neutropenia,
herein incorporated by	neutrophilia, psoriasis,
 reference in its entirety.	suppression of immune
Human dendritic cells that may	reactions to transplanted
be used according to these	organs and tissues,
assays may be isolated using	hemophilia, hypercoagulation,
techniques disclosed herein or	diabetes mellitus, endocarditis,
otherwise known in the art.	meningitis (bacterial and
Human dendritic cells are	viral), Lyme Disease, asthma,
antigen presenting cells in	and allergy Preferred
suspension culture, which,	indications also include
when activated by antigen	neoplastic diseases (e.g.,
and/or cytokines, initiate and	leukemia, lymphoma, and/or as
upregulate T cell proliferation	described below under
and functional activities.	"Hyperproliferative
	Disorders"). Highly preferred

					and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metanlasia, and/or dysplasia
411	HOEBK34	1359	CD152 in Human T cells		
411	HOEBK34	1359	Caspase (+paclitaxel) in SW480		
411	НОЕВК34	1359	IL-8 in SW480		
412	HOEBZ89	1360	Inhibition of squalene synthetase gene transcription.	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and	

SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1360
	HOEBZ89
	412

				active cells. 313-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	
412	HOEBZ89	1360	VEGF in HT1080		
412	HOEBZ89	1360	IgG in Human B cells SAC		
412	HOEBZ89	1360	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory	A highly preterred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

											_																		
and infection (e.g., viral infections tuberculosis	infections, tuociculosis, infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative
helper cell functions are well	I used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical
															=												100		
																					_								
						_,												_											

		approach" Chapter 6:138-160	Disorders"). Highly preferred
		(2000); Gonzalez et al., J Clin	indications include neoplasms
		Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
		Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
		Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
		et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
		15:749-795 (1997), and	esophageal, stomach, brain,
		Rheumatology (Oxford)	liver and urinary cancer. Other
		38(3):214-20 (1999), the	preferred indications include
		contents of each of which are	benign dysproliferative
		herein incorporated by	disorders and pre-neoplastic
		reference in its entirety.	conditions, such as, for
		Human T cells that may be	example, hyperplasia,
		used according to these assays	metaplasia, and/or dysplasia.
		may be isolated using	Preferred indications include
		techniques disclosed herein or	anemia, pancytopenia,
		otherwise known in the art.	leukopenia, thrombocytopenia,
		Human T cells are primary	Hodgkin's disease, acute
		human lymphocytes that	lymphocytic anemia (ALL),
		mature in the thymus and	plasmacytomas, multiple
		express a T Cell receptor and	myeloma, Burkitt's lymphoma,
		CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
		cells mediate humoral or cell-	disease, inflammatory bowel
		mediated immunity and may	disease, sepsis, neutropenia,
		be preactivated to enhance	neutrophilia, psoriasis,
		responsiveness to	suppression of immune
		immunomodulatory factors.	reactions to transplanted
			organs and tissues,
-			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,
	!		meningitis, Lyme Disease,

					asthma and allergy.
	HOEBZ89	1360	Production of IL-4	IL-4 FMAT. Assays for	A highly preferred
412				immunomodulatory proteins	embodiment of the invention
				secreted by TH2 cells that	includes a method for
				stimulate B cells, T cells,	stimulating (e.g., increasing)
				macrophages and mast cells	IL-4 production. An alternative
				and promote polarization of	highly preferred embodiment
				CD4+ cells into TH2 cells are	of the invention includes a
				well known in the art and may	method for inhibiting (e.g.,
				be used or routinely modified	reducing) IL-4 production.
				to assess the ability of	A highly preferred indication
				polypeptides of the invention	includes asthma. A highly
				(including antibodies and	preferred indication includes
-				agonists or antagonists of the	allergy. A highly preferred
				invention) to mediate	indication includes rhinitis.
				immunomodulation, stimulate	Additional highly preferred
				immune cells, modulate	indications include
				immune cell polarization,	inflammation and
				and/or mediate humoral or	inflammatory disorders.
				cell-mediated immunity.	Highly preferred indications
				Exemplary assays that test for	include neoplastic diseases
				immunomodulatory proteins	(e.g., leukemia, lymphoma,
				evaluate the production of	melanoma, and/or as described
				cytokines, such as IL-4, and	below under
				the stimulation of immune	"Hyperproliferative
				cells, such as B cells, T cells,	Disorders"). Preferred
				macrophages and mast cells.	indications include neoplasms
				Such assays that may be used	and cancers, such as, for
				or routinely modified to test	example, leukemia, lymphoma,
				immunomodulatory activity of	melanoma, and prostate,
				polypeptides of the invention	breast, lung, colon, pancreatic,

(including antibodies and	esophageal, stomach, brain,
agonists or antagonists of the	liver and urinary cancer. Other
invention) include the assays	preferred indications include
disclosed in Miraglia et al., J	benign dysproliferative
Biomolecular Screening 4:193-	disorders and pre-neoplastic
204 (1999); Rowland et al.,	conditions, such as, for
"Lymphocytes: a practical	example, hyperplasia,
approach" Chapter 6:138-160	metaplasia, and/or dysplasia.
(2000); Gonzalez et al., J Clin	Preferred indications include
Lab Anal 8(5):277-283 (1194);	blood disorders (e.g., as
Yssel et al., Res Immunol	described below under
144(8):610-616 (1993); Bagley	"Immune Activity", "Blood-
et al., Nat Immunol 1(3):257-	Related Disorders", and/or
261 (2000); and van der Graaff	"Cardiovascular Disorders").
et al., Rheumatology (Oxford)	Preferred indications include
38(3):214-220 (1999), the	autoimmune diseases (e.g.,
contents of each of which are	rheumatoid arthritis, systemic
herein incorporated by	lupus erythematosis, multiple
reference in its entirety.	sclerosis and/or as described
Human T cells that may be	below) and
used according to these assays	immunodeficiencies (e.g., as
may be isolated using	described below). Preferred
techniques disclosed herein or	indications include anemia,
otherwise known in the art.	pancytopenia, leukopenia,
Human T cells are primary	thrombocytopenia, Hodgkin's
human lymphocytes that	disease, acute lymphocytic
mature in the thymus and	anemia (ALL),
express a T cell receptor and	plasmacytomas, multiple
CD3, CD4, or CD8. These	myeloma, Burkitt's lymphoma,
cells mediate humoral or cell-	arthritis, AIDS, granulomatous
mediated immunity and may	disease, inflammatory bowel

				be preactivated to enhance responsiveness to immunomodulatory factors.	disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious
412	HOEBZ89	1360	IL-6 in HUVEC		
413	HOEDB32	1361	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate invention) to mediate immunomodulation, modulate T cell differentiation. Exemplary	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under

assavs that test for	"Immine Activity" "Blood-
imminomodulotomi neotoina	Doloted Disordons, and/or
Initiationalisations proteins	Related Disoluers, and/or
evaluate the production of	"Cardiovascular Disorders").
chemokines, such as	Highly preferred indications
macrophage inflammatory	include autoimmune diseases
protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
the activation of	systemic lupus erythematosis,
monocytes/macrophages and T	multiple sclerosis and/or as
cells. Such assays that may be	described below) and
used or routinely modified to	immunodeficiencies (e.g., as
test immunomodulatory and	described below). Additional
chemotaxis activity of	highly preferred indications
polypeptides of the invention	include inflammation and
(including antibodies and	inflammatory disorders.
agonists or antagonists of the	Preferred indications also
invention) include assays	include anemia, pancytopenia,
disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
Biomolecular Screening 4:193-	Hodgkin's disease, acute
204(1999); Rowland et al.,	lymphocytic anemia (ALL),
"Lymphocytes: a practical	plasmacytomas, multiple
approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,
(2000); Satthaporn and	arthritis, AIDS, granulomatous
Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
29 (2000); Verhasselt et al., J	suppression of immune
Immunol 158:2919-2925	reactions to transplanted
(1997); and Nardelli et al., J	organs and tissues, hemophilia,
Leukoc Biol 65:822-828	hypercoagulation, diabetes
(1999), the contents of each of	mellitus, endocarditis,
which are herein incorporated	meningitis, Lyme Disease,

				by reference in its entirety.	asthma, and allergy.
				Human dendritic cells that may	Preferred indications also
				be used according to these	include neoplastic diseases
				assays may be isolated using	(e.g., leukemia, lymphoma,
				techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
				suspension culture, which,	and cancers, such as, leukemia,
		•		when activated by antigen	lymphoma, prostate, breast,
-				and/or cytokines, initiate and	lung, colon, pancreatic,
				upregulate T cell proliferation	esophageal, stomach, brain,
				and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HOEDB32	1361	Production of TNF	TNFa FMAT. Assays for	A highly preferred
413			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications
				the ability of polypeptides of	include blood disorders (e.g.,

the invention (including and agonists or antagonists of the invention) to mediate inmunomodulation, modulate inflammation and ediate information and modulate inflammation and cytotoxicity. Exemplary immunomodulatory proteins cytokines such as tumor evaluate the production of cytokines such as tumor of an inflammatory or an inflammatory activity of inmunomodulatory activity of inflammatory disorders, and agonists or antagonists of the invention include assays that an approach. Total antagonist or antagonists of the invention include assays approach. Total antagonist or antagonists of antagonists or antagonists of antagonists or antagonists of antagonists of antagonists or antagonists of antagonist of antagonist of antagonists o	r con) to on, and ins ins ins it is it. I from it is it. I from it
the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 160(7):3585-3593	the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disiclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes, a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 18(11):388-3593 (2000); Verhasselt et al., Eur J Immunol 16(7):358-3593

.uml	Immunol 158:2919-2925	cancers, such as, leukemia,
(199	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
Leuk	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
(199	(1999), the contents of each of	tumors, and prostate, breast,
whic	which are herein incorporated	lung, colon, pancreatic,
by re	by reference in its entirety.	esophageal, stomach, brain,
Hum	Human dendritic cells that may	liver and urinary cancer. Other
pe us	be used according to these	preferred indications include
assay	assays may be isolated using	benign dysproliferative
techr	techniques disclosed herein or	disorders and pre-neoplastic
other	otherwise known in the art.	conditions, such as, for
Hum	Human dendritic cells are	example, hyperplasia,
antig	antigen presenting cells in	metaplasia, and/or dysplasia.
odsns	suspension culture, which,	Preferred indications include
wher	when activated by antigen	anemia, pancytopenia,
and/c	and/or cytokines, initiate and	leukopenia, thrombocytopenia,
) adn	upregulate T cell proliferation	Hodgkin's disease, acute
and f	and functional activities.	lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, Lyme Disease,
		cardiac reperfusion injury, and

HOEDB32 1361 Activation of transcription through the transcription transpared to the invention includes a method for inhibiting (e.g., reclusion) and may be used or as natural killer to a may be used or highly preferred embodiment to ealls). A preferred embodiment of general method for inhibiting (e.g., and may be used or highly preferred embodiment to a matural killer to a ballity of polypeptides of the invention includes a method for stimulating (e.g., and polypeptides and agonists or antagonists of the invention includes a method for stimulating (e.g., antagonists of the invention of the invention) to production. Preferred expression of genes in many cell types. Exemplary assays for many cell types. Exemplary assays for modulate the captor and agonists of the counting and agonists of the invention includes and agonists of the polypeptides of the counting the seases that may be used or routinely continued autoinmunue diseases that may be used or routinely continued and agonists or antagonists of the invention) included assays (e.g., rheumatoid arthritis, electrodical and agonists or antagonists of the invention) included assays (e.g., as described below).		HOEDB32	1361	MCP-1 in Eol-1		asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
transcription transcription transcription through the through serum response element in (SRE) are well-known in the recommend as natural killer routinely modified to assess cells). The ability of polypeptides of the invention (including matthodies and agonists or antagonists of the invention) to pregulate serum response in growth and upregulate the disconsist of genes in managonists of genes in world agenes in world genes in managonists of the invention) to transcription through the SRE in that may be used or routinely selectivity of the polypeptides of the invention (including antibodies selection) include assays (c.	413	000000000000000000000000000000000000000	•) 6 •			
through serum Serum Response Element response element in immune cells (such as natural killer routinely modified to assess cells). the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	413	HOEDB32	1361	Activation of transcription	Assays for the activation of transcription through the	A preferred embodiment of the invention includes a
ne cells (such art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays)			through serum	Serum Response Element	method for inhibiting (e.g.,
ne cells (such art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays				response element in	(SRE) are well-known in the	reducing) TNF alpha
ural killer routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays				immune cells (such	art and may be used or	production. An alternative
the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays				as natural killer	routinely modified to assess	highly preferred embodiment
· · · · · · · · · · · · · · · · · · ·				cells).	the ability of polypeptides of	of the invention includes a
					the invention (including	method for stimulating (e.g.,
					antibodies and agonists or	increasing) TNF alpha
S 8 4					antagonists of the invention) to	production. Preferred
e es					regulate serum response	indications include blood
E se					factors and modulate the	disorders (e.g., as described
es					expression of genes involved	below under "Immune
· · · · · · · · · · · · · · · · · · ·					in growth and upregulate the	Activity", "Blood-Related
					function of growth-related	Disorders", and/or
·				_	genes in many cell types.	"Cardiovascular Disorders"),
			_		Exemplary assays for	Highly preferred indications
					transcription through the SRE	include autoimmune diseases
					that may be used or routinely	(e.g., rheumatoid arthritis,
					modified to test SRE activity	systemic lupus erythematosis,
					of the polypeptides of the	Crohn"s disease, multiple
					invention (including antibodies	sclerosis and/or as described
					and agonists or antagonists of	below), immunodeficiencies
				,	the invention) include assays	(e.g., as described below),

																							•				
	suppressing a 1 centinediated immune response. Additional	highly preferred indications	include inflammation and inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for
disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson et al Timminol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.									

					example, hyperplasia,
					metanlasia and/or dysnlasia
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
		:			under "Infectious Disease").
	HOEDB32	1361	Activation of	Assays for the activation of	A highly preferred
413			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
	•		response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
			as T-cells).	well-known in the art and may	indications include

be used or routinely modified	inflammation and
to assess the ability of	inflammatory disorders.
polypeptides of the invention	Preferred indications include
(including antibodies and	blood disorders (e.g., as
agonists or antagonists of the	described below under
invention) to regulate STAT6	"Immune Activity", "Blood-
transcription factors and	Related Disorders", and/or
modulate the expression of	"Cardiovascular Disorders").
multiple genes. Exemplary	Preferred indications include
assays for transcription	autoimmune diseases (e.g.,
through the STAT6 response	rheumatoid arthritis, systemic
element that may be used or	lupus erythematosis, multiple
routinely modified to test	sclerosis and/or as described
STAT6 response element	below) and
activity of the polypeptides of	immunodeficiencies (e.g., as
the invention (including	described below).
antibodies and agonists or	Preferred indications include
antagonists of the invention)	neoplastic diseases (e.g.,
include assays disclosed in	leukemia, lymphoma,
Berger et al., Gene 66:1-10	melanoma, and/or as described
(1998); Cullen and Malm,	below under
Methods in Enzymol 216:362-	"Hyperproliferative
368 (1992); Henthorn et al.,	Disorders"). Preferred
Proc Natl Acad Sci USA	indications include neoplasms
85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
(1998); Moffatt et al.,	prostate, breast, lung, colon,
Transplantation 69(7):1521-	pancreatic, esophageal,
1523 (2000); Curiel et al., Eur	stomach, brain, liver and
J Immunol 27(8):1982-1987	urinary cancer. Other preferred
(1997): and Masuda et al J	indications include henion

				Biol Chem 275(38):29331-	dysproliferative disorders and
				29337 (2000), the contents of	pre-neoplastic conditions, such
				each of which are herein	as, for example, hyperplasia,
				incorporated by reference in its	metaplasia, and/or dysplasia.
				entirety. T cells that may be	Preferred indications include
				used according to these assays	anemia, pancytopenia,
				are publicly available (e.g.,	leukopenia, thrombocytopenia,
				through the ATCC).	Hodgkin's disease, acute
				Exemplary T cells that may be	lymphocytic anemia (ALL),
				used according to these assays	plasmacytomas, multiple
				include the SUPT cell line,	myeloma, Burkitt's lymphoma,
				which is a suspension culture	arthritis, AIDS, granulomatous
				of IL-2 and IL-4 responsive T	disease, inflammatory bowel
-				cells.	disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additional preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HOEDE28	1362	Production of TNF	TNFa FMAT. Assays for	A highly preferred
414			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An

		and other cell types that exert a	alternative highly preferred
		wide variety of inflammatory	embodiment of the invention
		and cytotoxic effects on a	includes a method for
		variety of cells are well known	stimulating (e.g., increasing)
		in the art and may be used or	TNF alpha production.
		routinely modified to assess	Highly preferred indications
	<u> </u>	the ability of polypeptides of	include blood disorders (e.g.,
 		the invention (including	as described below under
		antibodies and agonists or	"Immune Activity", "Blood-
 		antagonists of the invention) to	Related Disorders", and/or
		mediate immunomodulation,	"Cardiovascular Disorders"),
		modulate inflammation and	Highly preferred indications
		cytotoxicity. Exemplary	include autoimmune diseases
		assays that test for	(e.g., rheumatoid arthritis,
		immunomodulatory proteins	systemic lupus erythematosis,
		evaluate the production of	Crohn"s disease, multiple
		cytokines such as tumor	sclerosis and/or as described
-,-		necrosis factor alpha (TNFa),	below), immunodeficiencies
		and the induction or inhibition	(e.g., as described below),
		of an inflammatory or	boosting a T cell-mediated
		cytotoxic response. Such	immune response, and
		assays that may be used or	suppressing a T cell-mediated
		routinely modified to test	immune response. Additional
		immunomodulatory activity of	highly preferred indications
 -		polypeptides of the invention	include inflammation and
		(including antibodies and	inflammatory disorders, and
		agonists or antagonists of the	treating joint damage in
		invention) include assays	patients with rheumatoid
		disclosed in Miraglia et al., J	arthritis. An additional highly
		Biomolecular Screening 4:193-	preferred indication is sepsis.
		204(1999); Rowland et al.,	Highly preferred indications

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diseases: The phoma, and below iferative itionally, andications and leukemia,	ioma, glion lioma), so ate, breast, eatic, ach, brain, cancer. Oth ons include rative neoplastic	asia, for asia, r dysplasia ons include enia, abocytopen e, acute nia (ALL), nultiple 's lymphor ranulomatc ttory bowel nia, iasis,
include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, leukemia,	lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis,
includd (e.g., land/or under or Disord highly includd	lympho (e.g., n tumors lung, c esopha liver an preferr benign	conditi examp metapl Preferr anemic leukop Hodgk lymph plasme myelor arthriti disease disease
"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925	(1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or	otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.
1. L m (2.2 m (1.15) m (1.15) m (1.15)	(15) W (16) Hr.	Oth Hu and

414	HOEDE28 HOEDH84	1362	IL-10 in Human T- cell 2B9 Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6	suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectious Disease"). A highly preferred indication indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammatory disorders. Preferred indications include inflammatory disorders (e.g., as described below under "Immune Activity", "Blood-"Immune Activity", "Blood-"
				transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response	Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic

lupus erythematosis, multiple sclerosis and/or as described	immunodeficiencies (e.g., as described below).	Preferred indications include	neoplastic diseases (e.g.,	netanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,
element that may be used or routinely modified to test	activity of the polypeptides of the invention (including	antibodies and agonists or	antagonists of the invention)	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); Georas	et al., Blood 92(12):4529-4538	(1998); Moffatt et al.,	Transplantation 69(7):1521-	1523 (2000); Curiel et al., Eur	J Immunol 27(8):1982-1987	(1997); and Masuda et al., J	Biol Chem 275(38):29331-	29337 (2000), the contents of	each of which are herein	incorporated by reference in its	entirety. T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the SUPT cell line,
											_															

				which is a suspension culture of IL-2 and IL-4 responsive T cells.	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred infectious disease as described below under "Infectious Disease").
416	HOEFV61	1364	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include

antagonists of the invention) to	autoimmune diseases (e.g.,
regulate GATA3 transcription	rheumatoid arthritis, systemic
factors and modulate	lupus erythematosis, multiple
 expression of mast cell genes	sclerosis and/or as described
important for immune response	below) and
development. Exemplary	immunodeficiencies (e.g., as
assays for transcription	described below). Preferred
through the GATA3 response	indications include neoplastic
element that may be used or	diseases (e.g., leukemia,
routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
activity of polypeptides of the	pancreatic, esophageal,
invention (including antibodies	stomach, brain, liver, and
and agonists or antagonists of	urinary tract cancers and/or as
the invention) include assays	described below under
 disclosed in Berger et al., Gene	"Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);	Preferred indications include
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
contents of each of which are	lymphoma, arthritis, AIDS,
herein incorporated by	granulomatous disease,

				reference in its entirety. Mast cells that may be used	inflammatory bowel disease, sepsis, neutropenia.
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
_				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
416	HOEFV61	1364	VEGF in SW480		
į,	НОҒМQ33	1365	Regulation of	Assays for the regulation of	A highly preferred indication
417			viability and	viability and proliferation of	is diabetes mellitus. An
			proliferation of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
				the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
				regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
				cells. For example, the Cell	Disorders" section below),
				Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage

number of viable cells in	(e.g., due to diabetic
culture based on quantitation	neuropathy), blood vessel
of the ATP present which	blockage, heart disease, stroke,
signals the presence of	impotence (e.g., due to diabetic
metabolically active cells.	neuropathy or blood vessel
Exemplary assays that may be	blockage), seizures, mental
used or routinely modified to	confusion, drowsiness,
test regulation of viability and	nonketotic hyperglycemic-
proliferation of pancreatic beta	hyperosmolar coma,
cells by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Ohtani KI, et al.,	diseases and disorders as
Endocrinology, 139(1):172-8	described in the
(1998); Krautheim A, et al,	"Cardiovascular Disorders"
Exp Clin Endocrinol Diabetes,	section below), dyslipidemia,
107 (1):29-34 (1999), the	endocrine disorders (as
contents of each of which is	described in the "Endocrine
herein incorporated by	Disorders" section below),
reference in its entirety.	neuropathy, vision impairment
Pancreatic cells that may be	(e.g., diabetic retinopathy and
used according to these assays	blindness), ulcers and impaired
are publicly available (e.g.,	wound healing, and infection
through the ATCC) and/or	(e.g., infectious diseases and
may be routinely generated.	disorders as described in the
Exemplary pancreatic cells that	"Infectious Diseases" section
may be used according to these	below, especially of the
 assays include HITT15 Cells.	urinary tract and skin), carpal
HITT15 are an adherent	tunnel syndrome and
epithelial cell line established	Dupuytren's contracture). An

ese indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.		Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection) to (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include
from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.		Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, activation, and apoptosis.
	SEAP in Molt4/SRE	Activation of T-Cell p38 or JNK Signaling Pathway.
	1365	1366
	HOFMQ33	HOFMT75
·	417	418

Exemplar	Exemplary assays for JNK and	autoimmune diseases (e.g.,
p38 kinas		rheumatoid arthritis, systemic
or red or re	used or routinely modified to	lupus erythematosis, multiple
test JNK	test JNK and p38 kinase-	sclerosis and/or as described
induced a	induced activity of	below) and
polypepti	polypeptides of the invention	immunodeficiencies (e.g., as
(including	(including antibodies and	described below). Additional
agonists o	agonists or antagonists of the	highly preferred indications
invention	invention) include the assays	include inflammation and
disclosed	disclosed in Forrer et al., Biol	inflammatory disorders.
Chem 37	Chem 379(8-9):1101-1110	Highly preferred indications
(1998); G	(1998); Gupta et al., Exp Cell	also include neoplastic
Res 247(C	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
Kyriakis.	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
Symp 64:	Symp 64:29-48 (1999); Chang	below under
and Karin, Nature	ı, Nature	"Hyperproliferative
410(6824	410(6824):37-40 (2001); and	Disorders"). Highly preferred
Cobb MF	Cobb MH, Prog Biophys Mol	indications include neoplasms
Biol 71(3	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
the content	the contents of each of which	lymphoma, prostate, breast,
are herein	are herein incorporated by	lung, colon, pancreatic,
reference	reference in its entirety. T	esophageal, stomach, brain,
cells that	cells that may be used	liver, and urinary cancer. Other
according	according to these assays are	preferred indications include
publicly a	publicly available (e.g.,	benign dysproliferative
through tl	through the ATCC).	disorders and pre-neoplastic
Exemplar	Exemplary mouse T cells that	conditions, such as, for
may be us	-Se	example, hyperplasia,
assays inc	assays include the CTLL cell	metaplasia, and/or dysplasia.
line, whic	line, which is an IL-2	Preferred indications include
dependen	dependent suspension-culture	arthritis, asthma, AIDS,

				cell line with cytotoxic activity.	allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
418	HOFMT75	1366	Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation.

activity of polypeptides of the	embodiment of the invention
invention (including antibodies	includes a method for
and agonists or antagonists of	stimulating apoptosis of
the invention) include the	endothelial cells. An
assays disclosed in Forrer et	alternative highly preferred
al., Biol Chem 379(8-9):1101-	embodiment of the invention
1110 (1998); Gupta et al., Exp	includes a method for
Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
Soc Symp 64:29-48 (1999);	A highly preferred
Chang and Karin, Nature	embodiment of the invention
410(6824):37-40 (2001); and	includes a method for
Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
 the contents of each of which	alternative highly preferred
are herein incorporated by	embodiment of the invention
reference in its entirety.	includes a method for
Endothelial cells that may be	inhibiting (e.g., decreasing) the
used according to these assays	activation of and/or
are publicly available (e.g.,	inactivating endothelial cells.
through the ATCC).	A highly preferred
Exemplary endothelial cells	embodiment of the invention
that may be used according to	includes a method for
these assays include human	stimulating angiogenisis. An
umbilical vein endothelial cells	alternative highly preferred
(HUVEC), which are	embodiment of the invention
endothelial cells which line	includes a method for
venous blood vessels, and are	inhibiting angiogenesis. A
involved in functions that	highly preferred embodiment
include, but are not limited to,	of the invention includes a
angiogenesis, vascular	method for reducing cardiac

	permeability, vascular tone,	hypertrophy. An alternative
	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as
		described below under
		"Hyperproliferative
		Disorders"), and disorders of
-		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
	~~~	aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular
		disease, diabetic nephropathy,
		intracardiac shunt, cardiac
-		hypertrophy, myocardial
		infarction, chronic
 		hemodynamic overload, and/or
		as described below under
		"Cardiovascular Disorders").
		Highly preferred indications
		include cardiovascular,
		endothelial and/or angiogenic
		disorders (e.g., systemic
		disorders that affect vessels
		such as diabetes mellitus, as

well as diseases of the vessels	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,
																				-									

stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease,	hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and	lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as	wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring,

ischemia reperfusion injury,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lunus ervthematosis multiple
																		-	-										
																					-								
						_																	•						

sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	Highly preferred indications uction include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders.  Additional highly preferred indications include immune and hematopoietic disorders of the "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), tibodies are described below). Highly
	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis.  Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies).
	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
	1367
	HOFNC14
	419

		and agonists or antagonists of	include boosting or inhibiting
		the invention) include the	immune cell proliferation.
		assays disclosed in Forrer et	Preferred indications include
		al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
		1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
		Cell Res 247(2): 495-504	described below under
		(1999); Kyriakis JM, Biochem	"Hyperproliferative
		Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
		Chang and Karin, Nature	indications include boosting an
		410(6824):37-40 (2001); and	eosinophil-mediated immune
		Cobb MH, Prog Biophys Mol	response, and suppressing an
		Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
		the contents of each of which	response.
		are herein incorporated by	
		reference in its entirety.	
		Exemplary cells that may be	
		used according to these assays	
		include eosinophils.	
		Eosinophils are important in	
		the late stage of allergic	
		reactions; they are recruited to	
		tissues and mediate the	
		inflammatory response of late	
		stage allergic reaction.	
		Moreover, exemplary assays	
		that may be used or routinely	
		modified to assess the ability	
		of polypeptides of the	
		invention (including antibodies	
		and agonists or antagonists of	
	ļ	the invention) to modulate	

signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in	bronchial asthma is associated	with enhanced	phosyphorylation of JUN N-	terminal kinase and failure of	prednisolone to inhibit JUN N-	terminal kinase	phosphorylation" J Allergy	Clin Immunol; Sep;104(3 Pt	1):565-74 (1999); the contents
																	-													

				of each of which are herein	
				entirety.	
<del></del>	HOFND85	1368	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
		•		transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
		<del>.</del>		immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
	_			agonists or antagonists of the	under "Infectious Disease").
		-		invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative

	·	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	a	al., Virus Gnes 15(2):105-117	indications include neoplasms
_		(1997); and Fraser et al.,	and cancers, such
	2	29(3):838-844 (1999), the	as,melanoma, renal cell
	Ŏ	contents of each of which are	carcinoma, leukemia,
	Ч	herein incorporated by	lymphoma, and prostate,
	77	reference in its entirety. T	breast, lung, colon, pancreatic,
	<u> </u>	cells that may be used	esophageal, stomach, brain,
	<del>a</del>	according to these assays are	liver and urinary cancer. Other
	d	publicly available (e.g.,	preferred indications include
	17	through the ATCC).	benign dysproliferative
	ш	Exemplary human T cells that	disorders and pre-neoplastic
-	u	may be used according to these	conditions, such as, for
	ď	assays include the SUPT cell	example, hyperplasia,
	<u></u>	line, which is a suspension	metaplasia, and/or dysplasia.
	<u> </u>	culture of IL-2 and IL-4	Preferred indications also
	<u> </u>	responsive T cells.	include anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS,
			granulomatous disease,
•			inflammatory bowel disease,
			sepsis, neutropenia,
			neutrophilia, psoriasis,
			hemophilia, hypercoagulation,
_			diabetes mellitus, endocarditis,
			meningitis, Lyme Disease,
			suppression of immune

					reactions to transplanted
					organs, asthma and allergy.
	HOFNY91	1369	Activation of	Assays for the activation of	A preferred embodiment of
421			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
		_		the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
		-		Proc Natl Acad Sci USA	suppressing a T cell-mediated
				85:6342-6346 (1988); and	immune response. Additional
				Black et al., Virus Genes	highly preferred indications

	12(2):105-117 (1997). the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.
	publicly available (e.g.,	Highly preferred indications
	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below
	assays include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,
	dependent suspension culture	highly preferred indications
	of T cells with cytotoxic	include neoplasms and
	activity.	cancers, such as, for example,
		leukemia, lymphoma,
		melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,

					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
			!		under "Infectious Disease").
	HOFNY91	1369	Production of	Assays for measuring	Highly preferred indications
421			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
				agonists or antagonists of the	inflammatory disorders,
-				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and

				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
				endothelial cells. Endothelial	"Immune Activity", "Blood-
				cells are cells that line blood	Related Disorders",
				vessels, and are involved in	"Hyperproliferative Disorders"
				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
				endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other
				commercial sources. The	preferred indications include
				expression of VCAM	benign dysproliferative
				(CD106), a membrane-	disorders and pre-neoplastic
				associated protein, can be	conditions, such as, for
				upregulated by cytokines or	example, hyperplasia,
				other factors, and contributes	metaplasia, and/or dysplasia.
				to the extravasation of	
				lymphocytes, leucocytes and	
				other immune cells from blood	
				vessels; thus VCAM	
				expression plays a role in	
				promoting immune and	
				inflammatory responses.	
422	НОГОС33	1370	SEAP in ATP-3T3- 1 1		
	HOFOC33	1370	Activation of	Assays for the activation of	Highly preferred indications

122	transcription	transcription through the	include inflammation and
	through NFKB	NFKB response element are	inflammatory disorders.
	response element in	well-known in the art and may	Highly preferred indications
	immune cells (such	be used or routinely modified	include blood disorders (e.g.,
	as natural killer	to assess the ability of	as described below under
	cells).	polypeptides of the invention	"Immune Activity", "Blood-
		including antibodies and	Related Disorders", and/or
		agonists or antagonists of the	"Cardiovascular Disorders").
		invention) to regulate NFKB	Highly preferred indications
		transcription factors and	include autoimmune diseases
		modulate expression of	(e.g., rheumatoid arthritis,
		immunomodulatory genes.	systemic lupus erythematosis,
		Exemplary assays for	multiple sclerosis and/or as
		transcription through the	described below), and
		NFKB response element that	immunodeficiencies (e.g., as
		may be used or rountinely	described below). An
		modified to test NFKB-	additional highly preferred
		response element activity of	indication is infection (e.g.,
		polypeptides of the invention	AIDS, and/or an infectious
		(including antibodies and	disease as described below
		agonists or antagonists of the	under "Infectious Disease").
		invention) include assays	Highly preferred indications
		disclosed in Berger et al., Gene	include neoplastic diseases
		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
	-	216:362-368 (1992); Henthorn	below under
	-	et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Valle	Disorders"). Highly preferred
		Blazquez et al, Immunology	indications include neoplasms
		90(3):455-460 (1997);	and cancers, such as, for
		Aramburau et al., J Exp Med	example, melanoma, renal cell

				82(3):801-810 (1995); and Fraser et al., 29(3):838-844	carcinoma, leukemia, lymphoma, and prostate,
				(1999), the contents of each of	breast, lung, colon, pancreatic,
				which are herein incorporated	esophageal, stomach, brain,
				by reference in its entirety.	liver and urinary cancer. Other
				NK cells that may be used	preferred indications include
				according to these assays are	benign dysproliferative
				publicly available (e.g.,	disorders and pre-neoplastic
				through the ATCC).	conditions, such as, for
				Exemplary human NK cells	example, hyperplasia,
				that may be used according to	metaplasia, and/or dysplasia.
				these assays include the NKL	Preferred indications also
				cell line, which is a human	include anemia, pancytopenia,
				natural killer cell line	leukopenia, thrombocytopenia,
				established from the peripheral	Hodgkin's disease, acute
				blood of a patient with large	lymphocytic anemia (ALL),
				granular lymphocytic	plasmacytomas, multiple
				leukemia. This IL-2 dependent	myeloma, Burkitt's lymphoma,
		··		suspension culture cell line has	arthritis, AIDS, granulomatous
				a morphology resembling that	disease, inflammatory bowel
				of activated NK cells.	disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HOFOC73	1371	Myoblast cell		Highly preferred indications
423			proliferation	proliferation are well known in	include diabetes, myopathy,
				the art and may be used or	muscle cell atrophy, cancers of

		routinely modified to assess	muscle (such as,
		the ability of polypeptides of	rhabdomyoma, and
		the invention (including	rhabdosarcoma),
		antibodies and agonists or	cardiovascular disorders (such
		antagonists of the invention) to	as congestive heart failure,
_		stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
		cell proliferation. Exemplary	congenital cardiovascular
		assays for myoblast cell	abnormalities, heart disease,
		proliferation that may be used	cardiac arrest, heart valve
		or routinely modified to test	disease, vascular disease, and
	_	activity of polypeptides and	also as described below under
		antibodies of the invention	"Cardiovascular Disorders"),
		(including agonists or	stimulating myoblast
		antagonists of the invention)	proliferation, and inhibiting
. —		include, for example, assays	myoblast proliferation.
	_	disclosed in: Soeta, C., et al.	
		"Possible role for the c-ski	
		gene in the proliferation of	
		myogenic cells in regenerating	
		skeletal muscles of rats" Dev	
		Growth Differ Apr;43(2):155-	
		64 (2001); Ewton DZ, et al.,	
		"IGF binding proteins-4, -5	
		and -6 may play specialized	
		roles during L6 myoblast	
	_	proliferation and	
		differentiation" J Endocrinol	
		Mar;144(3):539-53 (1995);	
		and, Pampusch MS, et	
		al.,"Effect of transforming	
		growth factor beta on	

				proliferation of L6 and embryonic porcine myogenic cells" J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety.  Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	
423	H0F0C73	1371	Caspase (+camptothecin) in SW480		
424	HOGAW62	1372	Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention

0		
antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC).	antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC).	antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC).

			these assays include human	stimulating angiogenisis. An
			umbilical vein endothelial cells	alternative highly preferred
			(HUVEC), which are	embodiment of the invention
			endothelial cells which line	includes a method for
			venous blood vessels, and are	inhibiting angiogenesis. A
	_		involved in functions that	highly preferred embodiment
			include, but are not limited to,	of the invention includes a
		-	angiogenesis, vascular	method for reducing cardiac
			permeability, vascular tone,	hypertrophy. An alternative
			and immune cell extravasation.	highly preferred embodiment
				of the invention includes a
				method for inducing cardiac
				hypertrophy. Highly
				preferred indications include
				neoplastic diseases (e.g., as
				described below under
				"Hyperproliferative
	<u>.</u>			Disorders"), and disorders of
				the cardiovascular system
				(e.g., heart disease, congestive
	_			heart failure, hypertension,
				aortic stenosis,
				cardiomyopathy, valvular
				regurgitation, left ventricular
				dysfunction, atherosclerosis
				and atherosclerotic vascular
				disease, diabetic nephropathy,
	-			intracardiac shunt, cardiac
				hypertrophy, myocardial
				infarction, chronic
!				hemodynamic overload, and/or

angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery	disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as	Inrombophiebius, Iymphangitis, and Iymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly

		include tra wounds, b tissue (e.g such as, ir balloon ar atheroschl implant fi ischemia i rheumatoi cerebrova diseases s failure, an Additiona	include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, or afterection, diabetic or
		wounds, b tissue (e.g such as, ir balloon ar atheroschl implant fi ischemia r rheumatoi cerebrova diseases s failure, an Additiona indication	burns, and injured g., vascular injury njury resulting from ngioplasty, and nlerotic lesions), ixation, scarring, reperfusion injury, id arthritis, ascular disease, renal such as acute renal nd osteoporosis. al highly preferred ns include stroke, crion, diabetic or
		tissue (e.g. such as, ir balloon ar atheroschl implant fi ischemia rheumatoi cerebrova diseases s failure, an Additiona indication oraft reises	g., vascular injury njury resulting from ngioplasty, and nlerotic lesions), ixation, scarring, reperfusion injury, id arthritis, ascular disease, renal such as acute renal nd osteoporosis. al highly preferred ns include stroke, crion, diabetic or
		such as, ir balloon ar atheroschl implant fi ischemia rheumatoi cerebrova diseases s failure, an Additiona indication oraft rejectory	njury resulting from ngioplasty, and lerotic lesions), ixation, scarring, reperfusion injury, oid arthritis, ascular disease, renal such as acute renal nd osteoporosis. al highly preferred ns include stroke, crion, diabetic or
		balloon ar atheroschl implant fi ischemia i rheumatoi cerebrova diseases s failure, an Additiona indication	ngioplasty, and lerotic lesions), ixation, scarring, reperfusion injury, id arthritis, ascular disease, renal such as acute renal nd osteoporosis. al highly preferred is include stroke, crion, diabetic or
		atheroschi implant fi ischemia i rheumatoi cerebrova diseases s failure, an Additiona indication	interotic lesions), ixation, scarring, reperfusion injury, id arthritis, ascular disease, renal such as acute renal nd osteoporosis. al highly preferred is include stroke, crion, diabetic or
		implant fi ischemia i rheumatoi cerebrova diseases s failure, an Additiona indication	ixation, scarring, reperfusion injury, oid arthritis, ascular disease, renal such as acute renal nd osteoporosis.  al highly preferred is include stroke, crion, diabetic or
		ischemia i rheumatoi cerebrova diseases s failure, an Additiona indication	reperfusion injury, id arthritis, ascular disease, renal such as acute renal nd osteoporosis. al highly preferred as include stroke, crion, diabetic or
		rheumatoi cerebrova diseases s failure, an Additiona indication	ascular disease, renal such as acute renal nd osteoporosis. al highly preferred ns include stroke, crion, diabetic or
		cerebrova diseases s failure, an Additiona indication	sucular disease, renal such as acute renal nd osteoporosis. al highly preferred ns include stroke, crion, diabetic or
		diseases s failure, an Additiona indication	such as acute renal nd osteoporosis. al highly preferred ns include stroke, crion, diabetic or
_		failure, an Additiona indication	nd osteoporosis. al highly preferred as include stroke, ction, diabetic or
		Additiona indication oraft rejection	al highly preferred as include stroke, crion, diabetic or
		indication oraft rejection	ns include stroke, ction, diabetic or
		oraft reiec	ction, diabetic or
		ייניי יישים –	continuous from
		other retir	other retinopathies, thrombotic
		and coagu	and coagulative disorders,
		vascularit	vascularitis, lymph
		angiogene	angiogenesis, sexual disorders,
		age-relate	age-related macular
		degenerat	degeneration, and treatment
		/preventio	/prevention of endometriosis
		and relate	and related conditions.
		Additiona	Additional highly preferred
		indication	indications include fibromas,
		heart dise	heart disease, cardiac arrest,
		heart valv	heart valve disease, and
		vascular disease.	disease.
		Preferred	Preferred indications include
	!	blood disc	blood disorders (e.g., as

described below under "Immune Activity", "Blood- Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic	sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g	
		Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its
		Inhibition of squalene synthetase gene transcription.
		1373
		HOGCK20
	2555	425

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E - antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may
	Regulation of apoptosis of immune cells (such as mast cells).
	1373
	HOGCK20
	425

play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.	Immune cells that may be used	according to these assays are	publicly available (e.g.,	through commercial sources).	Exemplary immune cells that	may be used according to these	assays include mast cells such
												-											-							

				as the HMC human mast cell	
	HOGCK20	1373	IL-10 in Human T-cell 2B9		
	HOGCK20	1373	SEAP in OE-33		
	HOGCK63	1374	SEAP in		
_ <del></del>			HepG2/Squale- synthetase(stimulati on)		
	HOGCK63	1374	Production of	Assays for measuring	Preferred embodiments of the
_			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
_				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
		-		polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
_				that may be used or routinely	
_				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
_				al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	

used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).			RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediated immunity.  Exemplary assays that test for immunomodulatory proteins
	SEAP in HepG2/Squale- synthetase(stimulati on)	IL-2 in Human T cells	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1375	1375	1375
	HOGCS52	HOGCS52	HOGCS52
	427	427	2559

evaluate the production of	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human

ial cells line nd are at ted to, one, asation.	Highly preferred indications include inflammatory disorders.  It are inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g., and/or an infectious disease as described below and indication is infections.
umbilical vein-endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and
	Activation of transcription through NFKB response element in immune cells (such as T-cells).
	1375
	HOGCS52
	2561

	investion) include second	Highly meformed indications
	invention) include assays	Tilginiy picterited indications
	disclosed in Berger et al., Gene	include neoplastic diseases
	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
	 Malm, Methods in Enzymol	lymphoma, and/or as described
	216:362-368 (1992); Henthorn	below under
	 et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
-	 al., Virus Gnes 15(2):105-117	indications include neoplasms
	(1997); and Fraser et al.,	and cancers, such
	29(3):838-844 (1999), the	as,melanoma, renal cell
	 contents of each of which are	carcinoma, leukemia,
	herein incorporated by	lymphoma, and prostate,
	reference in its entirety. T	breast, lung, colon, pancreatic,
	 cells that may be used	esophageal, stomach, brain,
	according to these assays are	liver and urinary cancer. Other
	publicly available (e.g.,	preferred indications include
	 through the ATCC).	benign dysproliferative
	 Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	 assays include the SUPT cell	example, hyperplasia,
	line, which is a suspension	metaplasia, and/or dysplasia.
	 culture of IL-2 and IL-4	Preferred indications also
	 responsive T cells.	include anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS,
		granulomatous disease,
		inflammatory bowel disease,

					sepsis, neutropenia,
-					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
		·			diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HOHBB49	1376	Production of TNF	TNFa FMAT. Assays for	A highly preferred
428			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications
				the ability of polypeptides of	include blood disorders (e.g.,
				the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
				antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
				modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
				assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn"s disease, multiple
				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies

and	and the induction or inhibition	(e.g., as described below).
of	of an inflammatory or	boosting a T cell-mediated
cyt	cytotoxic response. Such	immune response, and
ass	assays that may be used or	suppressing a T cell-mediated
ron	routinely modified to test	immune response. Additional
ımı	immunomodulatory activity of	highly preferred indications
lod	polypeptides of the invention	include inflammation and
(ind	(including antibodies and	inflammatory disorders, and
agc	agonists or antagonists of the	treating joint damage in
vui	invention) include assays	patients with rheumatoid
dis	disclosed in Miraglia et al., J	arthritis. An additional highly
Bic	Biomolecular Screening 4:193-	preferred indication is sepsis.
707	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases
apr	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
(20	(2000); Verhasselt et al., Eur J	and/or as described below
Imi	Immunol 28(11):3886-3890	under "Hyperproliferative
(11)	(1198); Dahlen et al., J	Disorders"). Additionally,
Imi	Immunol 160(7):3585-3593	highly preferred indications
(19	(1998); Verhasselt et al., J	include neoplasms and
IMI	Immunol 158:2919-2925	cancers, such as, leukemia,
(19	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
Ter Pro-	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
(19	(1999), the contents of each of	tumors, and prostate, breast,
l wh	which are herein incorporated	lung, colon, pancreatic,
l ph	by reference in its entirety.	esophageal, stomach, brain,
- Hu	Human dendritic cells that may	liver and urinary cancer. Other
pe i	be used according to these	preferred indications include
ass	assays may be isolated using	benign dysproliferative
tec	techniques disclosed herein or	disorders and pre-neoplastic
oth	otherwise known in the art.	conditions, such as, for

				Human dendritic cells are	example, hyperplasia,
				antigen presenting cells in suspension culture, which,	metaplasia, and/or dysplasia. Preferred indications include
				when activated by antigen	anemia, pancytopenia,
				and/or cytokines, initiate and	leukopenia, thrombocytopenia,
				upregulate T cell proliferation	Hodgkin's disease, acute
				and functional activities.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
_					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
****	_				asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HOHBC68	1377	Activation of	Kinase assay. Kinase assays,	A highly preferred
429			Natural Killer Cell	for example an Elk-1 kinase	embodiment of the invention
			ERK Signaling	assay, for ERK signal	includes a method for
			Pathway.	transduction that regulate cell	stimulating natural killer cell
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment

	may be used or routinely	of the invention includes a
	modified to assess the ability	method for inhibiting natural
	of polypeptides of the	killer cell proliferation. A
	invention (including antibodies	highly preferred embodiment
-	and agonists or antagonists of	of the invention includes a
	the invention) to promote or	method for stimulating natural
	inhibit cell proliferation,	killer cell differentiation. An
	activation, and differentiation.	alternative highly preferred
	Exemplary assays for ERK	embodiment of the invention
	kinase activity that may be	includes a method for
	used or routinely modified to	inhibiting natural killer cell
	test ERK kinase-induced	differentiation. Highly
	activity of polypeptides of the	preferred indications include
	invention (including antibodies	neoplastic diseases (e.g., as
	and agonists or antagonists of	described below under
	the invention) include the	"Hyperproliferative
	assays disclosed in Forrer et	Disorders"), blood disorders
	al., Biol Chem 379(8-9):1101-	(e.g., as described below under
	1110 (1998); Kyriakis JM,	"Immune Activity",
	Biochem Soc Symp 64:29-48	"Cardiovascular Disorders",
	(1999); Chang and Karin,	and/or "Blood-Related
	Nature 410(6824):37-40	Disorders"), immune disorders
	(2001); and Cobb MH, Prog	(e.g., as described below under
	Biophys Mol Biol 71(3-4):479-	"Immune Activity") and
	500 (1999); the contents of	infections (e.g., as described
	each of which are herein	below under "Infectious
	incorporated by reference in its	Disease"). Preferred
	entirety. Natural killer cells	indications include blood
	that may be used according to	disorders (e.g., as described
	these assays are publicly	below under "Immune
	available (e.g., through the	Activity", "Blood-Related

V V	ATCC). Exemplary natural	Disorders", and/or
KI	killer cells that may be used	"Cardiovascular Disorders").
36	according to these assays	Highly preferred indications
.i.	include the human natural	include autoimmune diseases
Ki	killer cell lines (for example,	(e.g., rheumatoid arthritis,
2	NK-YT cells which have	systemic lupus erythematosis,
5	cytolytic and cytotoxic	multiple sclerosis and/or as
36	activity) or primary NK cells.	described below) and
		immunodeficiencies (e.g., as
		described below). Additional
		highly preferred indications
		include inflammation and
		inflammatory disorders.
		Highly preferred indications
		also include cancers such as,
		kidney, melanoma, prostate,
		breast, lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver, urinary cancer,
		lymphoma and leukemias.
		Other preferred indications
		include benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Other highly preferred
		indications include,
		pancytopenia, leukopenia,
		leukemias, Hodgkin's disease,
		acute lymphocytic anemia

					(ALL), arthritis, asthma,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, immune
					reactions to transplanted
					organs and tissues,
					endocarditis, meningitis, Lyme
					Disease, and allergies.
	HOHBY12	1378	Production of	Assays for measuring	Preferred embodiments of the
430			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Vascular Disease,
				invention) to regulate ICAM-1	Atherosclerosis, Restenosis,
				expression. Exemplary assays	Stroke, and Asthma.
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Rolfe BE, et al.,	
	-			Atherosclerosis, 149(1):99-110	
				(2000); Panettieri RA Jr, et al.,	
				J Immunol, 154(5):2358-2365	
				(1995); and, Grunstein MM, et	
				al., Am J Physiol Lung Cell	
				Mol Physiol, 278(6):L1154-	
				L1163 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	

HOHBY12 HOHBY12 HOHBY44	12 12 44	1378 1378 1379	IL-2 in Human T- cell 2B9 TNFa in Human T- cell 2B9 Activation of Adipocyte ERK Signaling Pathway	entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.  Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation,	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a
				Exemplary assays for ERK kinase activity that may be used or routinely modified to	embodiment of the invention includes a method for inhibiting adipocyte

1	test ERK kinase-induced	differentiation. A highly
	activity of polypeptides of the	dime
	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
1	the invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
7	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
1	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
I	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
	according to these assays	stroke, impotence and/or as
	include 3T3-L1 cells. 3T3-L1	described below under
	s an adherent mouse	"Immune Activity",
	preadipocyte cell line that is a	"Cardiovascular Disorders",
	continuous substrain of 3T3	and/or "Blood-Related

	fibroblast cells developed	Disorders"), immune disorders
	through clonal isolation and	(e.g., as described below under
	undergo a pre-adipocyte to	"Immune Activity"), neural
	adipose-like conversion under	disorders (e.g., as described
	appropriate differentiation	below under "Neural Activity
	conditions known in the art.	and Neurological Diseases"),
		and infection (e.g., as
 		described below under
		"Infectious Disease").
		A highly preferred indication
		is diabetes mellitus. An
		additional highly preferred
		indication is a complication
		associated with diabetes (e.g.,
		diabetic retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure,
		nephropathy and/or other
		diseases and disorders as
		described in the "Renal
		Disorders" section below),
		diabetic neuropathy, nerve
		disease and nerve damage
		(e.g., due to diabetic
		neuropathy), blood vessel
		blockage, heart disease, stroke,
		impotence (e.g., due to diabetic
		neuropathy or blood vessel
		blockage), seizures, mental
		confusion, drowsiness,
		nonketotic hyperglycemic-

		hyperosmolar coma
		cardiovascular disease (e o
	-	calulovascular discase (c.g.,
		heart disease, atheroscierosis,
		microvascular disease,
		hypertension, stroke, and other
		diseases and disorders as
		described in the
		"Cardiovascular Disorders"
		section below), dyslipidemia,
		endocrine disorders (as
		described in the "Endocrine
		Disorders" section below),
		neuropathy, vision impairment
		(e.g., diabetic retinopathy and
		blindness), ulcers and impaired
 -		wound healing, infection (e.g.,
		infectious diseases and
		disorders as described in the
		"Infectious Diseases" section
		below (particularly of the
		urinary tract and skin). An
		additional highly preferred
 		indication is obesity and/or
		complications associated with
		obesity. Additional highly
		preferred indications include
		weight loss or alternatively,
-		weight gain. Additional
		highly preferred indications are
		complications associated with
		insulin resistance.

	Addition	Additional nigniy preferred
	indication	indications are disorders of the
	mnscnlos	musculoskeletal systems
	including	including myopathies,
	muscular	muscular dystrophy, and/or as
	described herein.	herein.
	Addition	Additional highly preferred
	indication	indications include,
	hypertens	hypertension, coronary artery
	disease, c	disease, dyslipidemia,
	gallstone	gallstones, osteoarthritis,
	degenera	degenerative arthritis, eating
	disorders	disorders, fibrosis, cachexia,
	and kidne	and kidney diseases or
	disorders	disorders. Preferred
	indication	indications include neoplasms
	and cance	and cancer, such as,
	lymphon	lymphoma, leukemia and
	breast, cc	breast, colon, and kidney
	cancer. A	cancer. Additional preferred
	indication	indications include melanoma,
	prostate,	prostate, lung, pancreatic,
	esophage	esophageal, stomach, brain,
	liver, and	liver, and urinary cancer.
	Highly p	Highly preferred indications
	include li	include lipomas and
	liposarco	liposarcomas. Other preferred
	indication	indications include benign
	dysprolif	dysproliferative disorders and
	pre-neop	pre-neoplastic conditions, such
 	as, for ex	as, for example, hyperplasia,

432 HOHCC74 1380 432 HOHCC74 1380	Activation of Natural Killer C ERK Signaling Pathway.	15	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation,	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a
HOHCC74	Activatic Natural k ERK Sig Pathway		Cinase assay. Kinase assays, or example an Elk-1 kinase issay, for ERK signal ransduction that regulate cell proliferation or differentiation are well known in the art and nay be used or routinely nodified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or nhibit cell proliferation,	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a
432	Natural F ERK Sig Pathway		or example an Elk-1 kinase issay, for ERK signal ransduction that regulate cell ransduction or differentiation are well known in the art and nay be used or routinely nodified to assess the ability of polypeptides of the nvention (including antibodies and agonists or antagonists of the invention) to promote or nhibit cell proliferation,	embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a
	Pathway.		ransduction that regulate cell ransduction that regulate cell proliferation or differentiation are well known in the art and nay be used or routinely nodified to assess the ability of polypeptides of the nvention (including antibodies and agonists or antagonists of the invention) to promote or nhibit cell proliferation,	includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a
	Pathway		ransduction that regulate cell proliferation or differentiation ure well known in the art and nay be used or routinely nodified to assess the ability of polypeptides of the nvention (including antibodies and agonists or antagonists of the invention) to promote or nhibit cell proliferation,	stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a
			re well known in the art and nay be used or routinely nodified to assess the ability of polypeptides of the nvention (including antibodies and agonists or antagonists of the invention) to promote or nhibit cell proliferation,	proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a
			re well known in the art and nay be used or routinely nodified to assess the ability of polypeptides of the nvention (including antibodies and agonists or antagonists of the invention) to promote or nhibit cell proliferation,	highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a
		1. 1. 0. 1. 1.	nay be used or routinely nodified to assess the ability of polypeptides of the nvention (including antibodies and agonists or antagonists of he invention) to promote or nhibit cell proliferation,	of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a
		7 0 .11 8 17 .11	nodified to assess the ability of polypeptides of the nvention (including antibodies and agonists or antagonists of he invention) to promote or nhibit cell proliferation,	method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a
		1. 1. 2. 1. 2	of polypeptides of the nvention (including antibodies and agonists or antagonists of he invention) to promote or nhibit cell proliferation,	killer cell proliferation. A highly preferred embodiment of the invention includes a
		8 1	nvention (including antibodies and agonists or antagonists of he invention) to promote or nhibit cell proliferation,	highly preferred embodiment of the invention includes a
		1: t	ind agonists or antagonists of he invention) to promote or nhibit cell proliferation,	of the invention includes a
		1 1	he invention) to promote or nhibit cell proliferation,	
			nhibit cell proliferation,	method for stimulating natural
				killer cell differentiation. An
	_		activation, and differentiation.	alternative highly preferred
		1	Exemplary assays for ERK	embodiment of the invention
			kinase activity that may be	includes a method for
			used or routinely modified to	inhibiting natural killer cell
		<del></del>	test ERK kinase-induced	differentiation. Highly
			activity of polypeptides of the	preferred indications include
		• <b>••</b>	invention (including antibodies	neoplastic diseases (e.g., as
			and agonists or antagonists of	described below under
		<del>-</del>	the invention) include the	"Hyperproliferative
			assays disclosed in Forrer et	Disorders"), blood disorders
		-	al., Biol Chem 379(8-9):1101-	(e.g., as described below under
			1110 (1998); Kyriakis JM,	"Immune Activity",
			Biochem Soc Symp 64:29-48	"Cardiovascular Disorders",
		_	(1999); Chang and Karin,	and/or "Blood-Related
			Nature 410(6824):37-40	Disorders"), immune disorders

Biophys Mol Biol 71(3-4):4/9-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have eytolytic and cytotoxic activity) or primary NK cells.	infections (e.g., as described below under "Infectious helow under "Infectious cells Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases umple, e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Additional
son (1999); the conteres each of which are here incorporated by referentiated. Natural kille that may be used according available (e.g., throug ATCC). Exemplary r killer cells that may be according to these ass include the human nay killer cell lines (for exploytic and cytotoxi activity) or primary N extinity) or primary N	its to to
each of which are her incorporated by refere entirety. Natural kille that may be used acco these assays are publicated available (e.g., through ATCC). Exemplary result to the entire that may be according to these assinclude the human nat killer cell lines (for exployic and cytotoxicate) activity) or primary N activity) or primary N	to its s.
incorporated by referentirety. Natural kille that may be used accompanies as as as a seasy are publicated available (e.g., through ATCC). Exemplary resident that may be according to these as include the human natural killer cell lines (for exploration) or primary Nacytolytic and cytotoxicated activity) or primary Nacytotics.	its to to
entirety. Natural kille that may be used acco these assays are publiavailable (e.g., through ATCC). Exemplary register cells that may be according to these ass include the human nakiller cell lines (for exposition of the cytolytic and cytotoxia activity) or primary N	
that may be used acco these assays are public available (e.g., throug ATCC). Exemplary r killer cells that may b according to these ass include the human nai killer cell lines (for ex) NK-YT cells which h cytolytic and cytotoxi activity) or primary N	o s
these assays are publications available (e.g., through ATCC). Exemplary results that may be according to these assimplied the human natical lines (for example). NK-YT cells which he cytolytic and cytotoxications activity) or primary N	s
available (e.g., throug ATCC). Exemplary n killer cells that may b according to these ass include the human nat killer cell lines (for ey NK-YT cells which h cytolytic and cytotoxi activity) or primary N	.;
ATCC). Exemplary r killer cells that may b according to these ass include the human nal killer cell lines (for ex NK-YT cells which h cytolytic and cytotoxi activity) or primary N	· · · · · · · · · · · · · · · · · · ·
killer cells that may be according to these ass include the human nat killer cell lines (for ex NK-YT cells which he cytolytic and cytotoxi activity) or primary N	·
according to these ass include the human nat killer cell lines (for ex NK-YT cells which he cytolytic and cytotoxi activity) or primary N	ys rral mple, 'e
include the human nat killer cell lines (for ex NK-YT cells which h cytolytic and cytotoxi activity) or primary N	mple, //c
killer cell lines (for ex NK-YT cells which has cytolytic and cytotoxi activity) or primary N	mple,
NK-YT cells which h cytolytic and cytotoxi activity) or primary N	re cells.
eytolytic and cytotoxi activity) or primary N	cells.
activity) or primary N	
	immunodeficiencies (e.g., as described below). Additional
	described below). Additional
	highly preferred indications
	include inflammation and
_	inflammatory disorders.
	Highly preferred indications
	also include cancers such as,
	kidney, melanoma, prostate,
	breast, lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver, urinary cancer,
	lymphoma and leukemias.
	Other preferred indications
	include benign dysproliferative

disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.	
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays
	Activation of transcription through serum response element in immune cells (such as T-cells).
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	433

for transcription through the	Disorders", and/or
SRE that may be used or	
routinely modified to test CDE	
o seriou community of the market of	
activity of the polypeptides of	
the invention (including	(e.g., rheumatoid arthritis,
antibodies and agonists or	
antagonists of the invention)	
include assays disclosed in	sclerosis and/or as described
Berger et al., Gene 66:1-10	below), immunodeficiencies
(1998); Cullen and Malm,	(e.g., as described below),
Methods in Enzymol 216:362-	
368 (1992); Henthorn et al.,	immune response, and
Proc Natl Acad Sci USA	suppressing a T cell-mediated
85:6342-6346 (1988); and	immune response. Additional
Black et al., Virus Genes	highly preferred indications
12(2):105-117 (1997), the	include inflammation and
 content of each of which are	inflammatory disorders, and
herein incorporated by	treating joint damage in
reference in its entirety. T	patients with rheumatoid
cells that may be used	arthritis. An additional highly
according to these assays are	preferred indication is sepsis.
 publicly available (e.g.,	Highly preferred indications
through the ATCC).	include neoplastic diseases
Exemplary mouse T cells that	at (e.g., leukemia, lymphoma,
may be used according to these	
assays include the CTLL cell	
 line, which is an IL-2	Disorders"). Additionally,
dependent suspension culture	e highly preferred indications
of T cells with cytotoxic	include neoplasms and
activity.	cancers, such as, for example,
	leukemia, lymphoma,

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	1:
	 mailgnant giloma), solid
	tumors, and prostate, breast,
	lung, colon, pancreatic,
 	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	 benign dysproliferative
	disorders and pre-neoplastic
	conditions, such as, for
	example, hyperplasia,
	metaplasia, and/or dysplasia.
	Preferred indications include
	 anemia, pancytopenia,
	leukopenia, thrombocytopenia,
	 Hodgkin's disease, acute
	lymphocytic anemia (ALL),
	 plasmacytomas, multiple
	 myeloma, Burkitt's lymphoma,
	 arthritis, AIDS, granulomatous
	disease, inflammatory bowel
 	disease, neutropenia,
	neutrophilia, psoriasis,
	suppression of immune
	reactions to transplanted
 	organs and tissues,
	hemophilia, hypercoagulation,
	diabetes mellitus, endocarditis,
	meningitis, Lyme Disease,
	cardiac reperfusion injury, and
	asthma and allergy. An

					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HONAH29	1382	Activation of	This reporter assay measures	Highly preferred indications
434			transcription	activation of the GATA-3	include allergy, asthma, and
_			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred
				through the GATA3 response	indications include neoplastic
				element that may be used or	diseases (e.g., leukemia,
				routinely modified to test	lymphoma, melanoma,
				GATA3-response element	prostate, breast, lung, colon,

	of the action of the	Increasing contractor
	activity of polypeptides of the	pancicanic, esopinageai,
	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
-	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred
	Malm, Methods in Enzymol	indications include benign
	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Quant Biol 64:563-571 (1999);	Preferred indications include
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
	Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
	contents of each of which are	lymphoma, arthritis, AIDS,
	herein incorporated by	granulomatous disease,
	reference in its entirety. Mast	inflammatory bowel disease,
	cells that may be used	sepsis, neutropenia,
	according to these assays are	neutrophilia, psoriasis,
	publicly available (e.g.,	suppression of immune
	through the ATCC).	reactions to transplanted
	Exemplary human mast cells	organs and tissues, hemophilia,
	that may be used according to	hypercoagulation, diabetes
	these assays include the HMC-	mellitus, endocarditis,
	1 cell line, which is an	meningitis, and Lyme Disease.
	immature human mast cell line	
	established from the peripheral	

				blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	
434	HONAH29	1382	Activation of transcription	This reporter assay measures activation of the NFAT	Highly preferred indications include allergy, asthma, and
			through NFAT response element in	signaling pathway in HMC-1 human mast cell line.	rhinitis. Additional preferred indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast coms).	cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic
				transcription through the	diseases (e.g., leukemia,
				NFAT response element that	lymphoma, melanoma,
				may be used or routinely	prostate, breast, lung, colon,

	modified to test NFAT-	pancreatic, esophageal,
	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	 31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
	which are herein incorporated	sepsis, neutropenia,
	by reference in its entirety.	neutrophilia, psoriasis,
	Mast cells that may be used	suppression of immune
	according to these assays are	reactions to transplanted
	publicly available (e.g.,	organs and tissues, hemophilia,
	through the ATCC).	hypercoagulation, diabetes
	Exemplary human mast cells	mellitus, endocarditis,
	that may be used according to	meningitis, and Lyme Disease.
	these assays include the HMC-	
	I cell line, which is an	

HOSDJ25

				are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.	
435	HOSDJ25	1383	SEAP in HIB/CRE		
	HOSDJ25	1383	Activation of	Assays for the activation of	Highly preferred indications
435			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated I	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
	-			and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An

	polypeptides of the invention	additional highly preferred
	(including antibodies and	indication is infection (e.g., an
	agonists or antagonists of the	infectious disease as described
	invention) include assays	below under "Infectious
	disclosed in Berger et al., Gene	Disease"). Preferred
	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988);	"Hyperproliferative
	Aramburu et al., J Exp Med	Disorders"). Preferred
	182(3):801-810 (1995); De	indications include neoplasms
	Boer et al., Int J Biochem Cell	and cancers, such as, for
	Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
-	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. NK	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,
	according to these assays are	metaplasia, and/or dysplasia.
	publicly available (e.g.,	Preferred indications also
	through the ATCC).	include anemia, pancytopenia,
	Exemplary human NK cells	leukopenia, thrombocytopenia,
	that may be used according to	Hodgkin's disease, acute
	these assays include the NK-	lymphocytic anemia (ALL),
	YT cell line, which is a human	plasmacytomas, multiple
	natural killer cell line with	myeloma, Burkitt's lymphoma,
	cytolytic and cytotoxic	arthritis, AIDS, granulomatous

				activity.	disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
	-				diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HOSDJ25	1383	Regulation of	Caspase Apoptosis. Assays	A highly preferred
435			apoptosis in	for caspase apoptosis are well	indication is diabetes mellitus.
			pancreatic beta	known in the art and may be	An additional highly preferred
			cells.	used or routinely modified to	indication is a complication
	·····			assess the ability of	associated with diabetes (e.g.,
				polypeptides of the invention	diabetic retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to promote caspase	nephropathy and/or other
				protease-mediated apoptosis.	diseases and disorders as
				Apoptosis in pancreatic beta is	described in the "Renal
				associated with induction and	Disorders" section below),
				progression of diabetes.	diabetic neuropathy, nerve
				Exemplary assays for caspase	disease and nerve damage
				apoptosis that may be used or	(e.g., due to diabetic
				routinely modified to test	neuropathy), blood vessel
				capase apoptosis activity of	blockage, heart disease, stroke,
				polypeptides of the invention	impotence (e.g., due to diabetic
				(including antibodies and	neuropathy or blood vessel
				agonists or antagonists of the	blockage), seizures, mental
				invention) include the assays	confusion, drowsiness,

disclosed in:	disclosed in: Loweth, AC, et	nonketotic hyperglycemic-
al., FEBS Le	al., FEBS Lett, 400(3):285-8	hyperosmolar coma,
(1997); Saini, KS, et al.,	, KS, et al.,	cardiovascular disease (e.g.,
Biochem Mol Biol Int,	l Biol Int,	heart disease, atherosclerosis,
39(6):1229-36 (1996);	6 (1996);	microvascular disease,
Krautheim, A., et al., Br J	λ., et al., Br J	hypertension, stroke, and other
Pharmacol, 1	Pharmacol, 129(4):687-94	diseases and disorders as
(2000); Chandra J, et al.,	dra J, et al.,	described in the
Diabetes, 50	Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"
(2001); Suk K, et al., J	ζ, et al., J	section below), dyslipidemia,
Immunol, 166(7):4481-9	6(7):4481-9	endocrine disorders (as
(2001); Tejec	(2001); Tejedo J, et al., FEBS	described in the "Endocrine
Lett, 459(2):	Lett, 459(2):238-43 (1999);	Disorders" section below),
Zhang, S., et	Zhang, S., et al., FEBS Lett,	neuropathy, vision impairment
455(3):315-2	455(3):315-20 (1999); Lee et	(e.g., diabetic retinopathy and
al., FEBS Le	al., FEBS Lett 485(2-3): 122-	blindness), ulcers and impaired
126 (2000); 1	126 (2000); Nor et al., J Vasc	wound healing, and infection
Res 37(3): 2(	Res 37(3): 209-218 (2000);	(e.g., infectious diseases and
and Karsan and Harlan, J	nd Harlan, J	disorders as described in the
Atheroscler	Atheroscler Thromb 3(2): 75-	"Infectious Diseases" section
80 (1996); th	80 (1996); the contents of each	below, especially of the
of which are herein	herein	urinary tract and skin), carpal
incorporated	incorporated by reference in its	tunnel syndrome and
entirety. Par	entirety. Pancreatic cells that	Dupuytren's contracture).
may be used	may be used according to these	An additional highly preferred
assays are pu	assays are publicly available	indication is obesity and/or
(e.g., through the ATCC)	the ATCC)	complications associated with
and/or may be routinely	e routinely	obesity. Additional highly
generated. Exemplary	xemplary	preferred indications include
pancreatic ce	pancreatic cells that may be	weight loss or alternatively,
used accordi	used according to these assays	weight gain. Aditional

ex	expression level is strongly	"Cardiovascular Disorders"),
a.	regulated by cytokines, growth	and infection (e.g., as
fa	factors, and hormones are well	described below under
kr	known in the art and may be	"Infectious Disease"). Highly
sn	used or routinely modified to	preferred indications include
as	assess the ability of	autoimmune diseases (e.g.,
od -	polypeptides of the invention	rheumatoid arthritis, systemic
ij)	(including antibodies and	lupus erythematosis, multiple
226	agonists or antagonists of the	sclerosis and/or as described
ui	invention) to mediate	below) and
ni	immunomodulation and	immunodeficiencies (e.g., as
. di	differentiation and modulate T	described below). Highly
a	cell proliferation and function.	preferred indications also
E	Exemplary assays that test for	include boosting a B cell-
ui.	immunomodulatory proteins	mediated immune response
ev ev	evaluate the production of	and alternatively suppressing a
cy	cytokines, such as IL-6, and	B cell-mediated immune
th	the stimulation and	response. Highly preferred
in	upregulation of T cell	indications include
pr	proliferation and functional	inflammation and
ac	activities. Such assays that	inflammatory
u -	may be used or routinely	disorders. Additional highly
u —	modified to test	preferred indications include
ni	immunomodulatory and	asthma and allergy. Highly
- di	diffferentiation activity of	preferred indications include
Dd .	polypeptides of the invention	neoplastic diseases (e.g.,
ii)	(including antibodies and	myeloma, plasmacytoma,
ag	agonists or antagonists of the	leukemia, lymphoma,
ii	invention) include assays	melanoma, and/or as described
G	disclosed in Miraglia et al., J	below under
B	Biomolecular Screening 4:193-	"Hyperproliferative

204(1999); Rowland et al.,	Disorders"). Highly preferred indications include neoplasms
	and cancers, such as, myeloma,
al., J	plasmacytoma, leukemia,
	lymphoma, melanoma, and
(1997), the contents of each of   p	prostate, breast, lung, colon,
which are herein incorporated   p	pancreatic, esophageal,
by reference in its entirety.	stomach, brain, liver and
Human dendritic cells that may under the may under the max	urinary cancer. Other preferred
be used according to these	indications include benign
assays may be isolated using d	dysproliferative disorders and
techniques disclosed herein or   p	pre-neoplastic conditions, such
otherwise known in the art.	as, for example, hyperplasia,
Human dendritic cells are	metaplasia, and/or dysplasia.
antigen presenting cells in F	Preferred indications include
	anemia, pancytopenia,
	leukopenia, thrombocytopenia,
and/or cytokines, initiate and   I	Hodgkin's disease, acute
	lymphocytic anemia (ALL),
and functional activities.	multiple myeloma, Burkitt's
	lymphoma, arthritis, AIDS,
53	granulomatous disease,
	inflammatory bowel disease,
S	sepsis, neutropenia,
	neutrophilia, psoriasis,
S	suppression of immune
	reactions to transplanted
	organs and tissues,
	hemophilia, hypercoagulation,
	diabetes mellitus, endocarditis,
	meningitis, and Lyme Disease.

					An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
437	HOSFD58	1385	Activation of T-Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, activation, and apoptosis.  Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic

		Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
		Kyriakis JM, Biochem Soc	lymphoma, and/or as described
		Symp 64:29-48 (1999); Chang	below under
		and Karin, Nature	"Hyperproliferative
		410(6824):37-40 (2001); and	Disorders"). Highly preferred
		Cobb MH, Prog Biophys Mol	indications include neoplasms
		Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
		the contents of each of which	lymphoma, prostate, breast,
		are herein incorporated by	lung, colon, pancreatic,
		reference in its entirety. T	esophageal, stomach, brain,
		cells that may be used	liver, and urinary cancer. Other
		according to these assays are	preferred indications include
		publicly available (e.g.,	benign dysproliferative
		through the ATCC).	disorders and pre-neoplastic
		Exemplary mouse T cells that	conditions, such as, for
-		may be used according to these	example, hyperplasia,
		assays include the CTLL cell	metaplasia, and/or dysplasia.
		line, which is an IL-2	Preferred indications include
		dependent suspension-culture	arthritis, asthma, AIDS,
		cell line with cytotoxic	allergy, anemia, pancytopenia,
		activity.	leukopenia, thrombocytopenia,
			Hodgkin"s disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt"s lymphoma,
			granulomatous disease,
			inflammatory bowel disease,
			sepsis, psoriasis, suppression
			of immune reactions to
			transplanted organs and
			tissues, endocarditis,

					meningitis, and Lyme Disease.
470	ноисо17	1386	Activation of	Kinase assay. Kinase assays,	A highly preferred
428			Adipocyte EKK	Ior example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for EKK signal	includes a method for
		-		transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
				inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
				test ERK kinase-induced	differentiation. A highly
				activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
	-			and agonists or antagonists of	for stimulating (e.g.,
				the invention) include the	increasing) adipocyte
				assays disclosed in Forrer et	activation. An alternative
				al., Biol Chem 379(8-9):1101-	highly preferred embodiment
				1110 (1998); Le Marchand-	of the invention includes a
				Brustel Y, Exp Clin	method for inhibiting the
				Endocrinol Diabetes	activation of (e.g., decreasing)
				107(2):126-132 (1999);	and/or inactivating adipocytes.
				Kyriakis JM, Biochem Soc	Highly preferred indications
				Symp 64:29-48 (1999); Chang	include endocrine disorders

and Karin, Nature	(e.g., as described below under
410(6824):37-40 (2001): and	"Endocrine Disorders").
Cobb MH Prog Biophys Mol	Highly preferred indications
Biol 71(3-4):479-500 (1999);	also include neoplastic
the contents of each of which	diseases (e.g., lipomas,
are herein incorporated by	liposarcomas, and/or as
reference in its entirety.	described below under
Mouse adipocyte cells that	"Hyperproliferative
may be used according to these	Disorders"). Preferred
assays are publicly available	indications include blood
(e.g., through the ATCC).	disorders (e.g., hypertension,
Exemplary mouse adipocyte	congestive heart failure, blood
cells that may be used	vessel blockage, heart disease,
according to these assays	stroke, impotence and/or as
include 3T3-L1 cells. 3T3-L1	described below under
is an adherent mouse	"Immune Activity",
preadipocyte cell line that is a	"Cardiovascular Disorders",
continuous substrain of 3T3	and/or "Blood-Related
fibroblast cells developed	Disorders"), immune disorders
through clonal isolation and	(e.g., as described below under
undergo a pre-adipocyte to	"Immune Activity"), neural
adipose-like conversion under	disorders (e.g., as described
appropriate differentiation	below under "Neural Activity
conditions known in the art.	and Neurological Diseases"),
	and infection (e.g., as
	described below under
	"Infectious Disease").
	A highly preferred indication
	is diabetes mellitus. An
	additional highly preferred
	indication is a complication

diabetic retinopathy, diabetic nephropathy, diabetic nephropathy, diabetic nephropathy, diabetic nephropathy, advor other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy, blood vessel blockage, seizurus, mental confusion, drowsiness, nonkcotic hyperglycentic—hypersomalar coma, arathovascular disease, atherosclerosis, microvascular disease, apprentiation, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dysilpidemia, endocrine disorders (as eleaserbed in the "Endocrine Disorders (as eleaserbed in the "Endocrine Disorders (as eleaserbed in the "Indocrine disorders (as eleaserbed in the "Indocrine disorders (as eleaserbed in the "Indocrine disorders (as eleaserbed in the view in perupathy, vision inpatiment neuropathy, vision inpatiment neuropathy, vision inpatiment neuropathy, or in inpatiment neuropathy, or in indiament neuropathy, or indiament neuropathy, indiament neuropathy, indiament neuropathy, indiament neu	associated with diabetes (e.g.,	diabetes (e.g.,
(e.g., renal failure,	diabetic retinopa	athy, diabetic
(e.g., renal failure, nephropathy and for other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy oblood vessel blockage, heart disease, stoke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage, seizures, mental confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., hypertonsion, stocke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment neuropathy, vision impairment	nephropathy, kid	idney disease
diseases and disorders as described in the "Renal Disorders" section below, diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage, perizures, mental confusion, drowsiness, nonketotic hyperglycemic— hypercamolar coma, cardiovascular disease, alherosclerosis, microvascular disease, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	(e.g., renal failur	ıre,
diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy) blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental conflusion, drowsiness, nonketotic hyperglycemic—hyperosmolar coma, cardiovascular disease, theart disease, atherosclerosis, microvascular disease, thypertension, stroke, and other diseases and disorders as described in the "Cardiovascular disease, section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment neuropathy, vision impairment	nephropathy and	d/or other
described in the "Renal Disorders" section below, diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage, peart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage, seizures, mental confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease, hypertension, stroke, and other diseases and disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	diseases and disc	sorders as
Disorders" section below), diabetic neuropathy, nerve disease and nerve danage (e.g., due to diabetic neuropathy, blood vessel blockage, hart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hypergycemic- hyperosmolar coma, cardiovascular disease, e.g., heart disease, afteroselerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	described in the	e "Renal
diabetic neuropathy, nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atheroselerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	Disorders" section	ion below),
disease and nerve damage  (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	diabetic neuropa	athy, nerve
(e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atheroselerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	disease and nerv	ve damage
neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders' section below), neuropathy, vision impairment	(e.g., due to diab	lbetic
blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atheroselerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), handorine Disorders" section below), neuropathy, vision impairment	neuropathy), blo	ood vessel
impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hypergylycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below, dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment neuropathy, vision impairment	 blockage, heart c	disease, stroke,
neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	impotence (e.g.,	, due to diabetic
blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic—hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	neuropathy or bl	lood vessel
confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	blockage), seizur	ures, mental
nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	confusion, drow	vsiness,
hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	nonketotic hyper	erglycemic-
cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), hypertension impairment neuropathy, vision impairment	hyperosmolar co	oma,
heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders (as described in the "Endocrine Disorders") section below), neuropathy, vision impairment	cardiovascular d	disease (e.g.,
microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	heart disease, at	therosclerosis,
hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	microvascular di	lisease,
diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	hypertension, str	troke, and other
described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	diseases and dise	sorders as
"Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	described in the	0
section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	"Cardiovascular	r Disorders"
endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	section below), o	dyslipidemia,
described in the "Endocrine Disorders" section below), neuropathy, vision impairment	endocrine disord	ders (as
Disorders" section below), neuropathy, vision impairment	described in the	"Endocrine
neuropathy, vision impairment	Disorders" section	ion below),
	neuropathy, visi	ion impairment

	(e.g. diabetic retinonathy and
 	blindness), ulcers and impaired
	wound healing, infection (e.g.,
	infectious diseases and
 	 disorders as described in the
 	"Infectious Diseases" section
	below (particularly of the
	urinary tract and skin). An
	additional highly preferred
	 indication is obesity and/or
	complications associated with
	obesity. Additional highly
	preferred indications include
	weight loss or alternatively,
	weight gain. Additional
	highly preferred indications are
	complications associated with
	insulin resistance.
	Additional highly preferred
	 indications are disorders of the
	musculoskeletal systems
	 including myopathies,
	muscular dystrophy, and/or as
	described herein.
	Additional highly preferred
	indications include,
	hypertension, coronary artery
	disease, dyslipidemia,
	gallstones, osteoarthritis,
	degenerative arthritis, eating
	disorders, fibrosis, cachexia,

and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia.		Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
		Kinase assays, for example an Elk-1 kinase assay for ERK signal transduction that regulates cell proliferation or differentiation, are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or
	SEAP in HIB/CRE	Regulation of proliferation and/or differentiation in immune cells (such as mast cells).
	1386	1386
	HOUCQ17	HOUCQ17
	438	438

antagonists of the invention) to	promote or inhibit cell	proliferation, activation, and	differentiation. Exemplary	assays for ERK kinase activity	that may be used or routinely	modified to test ERK kinase-	induced activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in: Ali H, et al., J	Immunol, 165(12):7215-7223	(2000); Tam SY, et al., Blood,	90(5):1807-1820 (1997);	Forrer et al., Biol Chem 379(8-	9):1101-1110 (1998); Berra et	al., Biochem Pharmacol	60(8):1171-1178 (2000);	Gupta et al., Exp Cell Res	247(2):495-504 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary immune cells that	may be used according to these
										-																				

				assays include human mast	
				cells such as the HMC-1 cell line.	
	HOUCQ17	1386	Activation of	This reporter assay measures	Highly preferred indications
438			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
			-	production. Assays for the	inflammation and
			-	activation of transcription	inflammatory disorders.
		-		through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
	_			regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred
				through the GATA3 response	indications include neoplastic
				element that may be used or	diseases (e.g., leukemia,
				routinely modified to test	lymphoma, melanoma,
				GATA3-response element	prostate, breast, lung, colon,
				activity of polypeptides of the	pancreatic, esophageal,

	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred
	Malm, Methods in Enzymol	indications include benign
	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Quant Biol 64:563-571 (1999);	Preferred indications include
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
	Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
	contents of each of which are	lymphoma, arthritis, AIDS,
	herein incorporated by	granulomatous disease,
	reference in its entirety. Mast	inflammatory bowel disease,
	cells that may be used	sepsis, neutropenia,
	according to these assays are	neutrophilia, psoriasis,
	publicly available (e.g.,	suppression of immune
	through the ATCC).	reactions to transplanted
	Exemplary human mast cells	organs and tissues, hemophilia,
	that may be used according to	hypercoagulation, diabetes
	these assays include the HMC-	mellitus, endocarditis,
	1 cell line, which is an	meningitis, and Lyme Disease.
	immature human mast cell line	
	established from the peripheral	
	blood of a patient with mast	

				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HOUCQ17	1386	Activation of	This reporter assay measures	Highly preferred indications
438			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
		·		modulate expression of genes	below) and
		-		involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic
				transcription through the	diseases (e.g., leukemia,
				NFAT response element that	lymphoma, melanoma,
				may be used or routinely	prostate, breast, lung, colon,
				modified to test NFAT-	pancreatic, esophageal,

	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
	which are herein incorporated	sepsis, neutropenia,
	by reference in its entirety.	neutrophilia, psoriasis,
	Mast cells that may be used	suppression of immune
	according to these assays are	reactions to transplanted
	publicly available (e.g.,	organs and tissues, hemophilia,
 	through the ATCC).	hypercoagulation, diabetes
	Exemplary human mast cells	mellitus, endocarditis,
	that may be used according to	meningitis, and Lyme Disease.
	these assays include the HMC-	
	1 cell line, which is an	
	immature human mast cell line	

established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed
	Proliferation of preadipose cells (such as 3T3-L1 cells)
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	438

through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.					RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cell-mediated immunity.
	IgG in Human B cells SAC	IFNg in Human T- cell 2B9	IL-10 in Human T- cell 2B9	IL-6 in HUVEC	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1386	1386	1386	1386	1386
	ноисо17	HOUCQ17	HOUCQ17	НОССФ17	HOUCQ17
	438	438	438	438	438

hat test for	proteins tion of	AANTES,		ses in	n assays	routinely		activity of	invention	es and	ists of the	he assays	ia et al., J	ning 4:193-	nd et al.,	actical	6:138-160	I., Science	15 (1995);	, Clin Exp	8-407	s of each of	corporated	artirety.	at may be	nese assays	le (e.g.,		lial cells
Exemplary assays that test for	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells

ells re re ro,		A highly preferred indication is allergy.  Another highly preferred indication is asthma.  Additional highly preferred inflammation and inflammation and inflammatory disorders.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").  Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple
that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.		Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or
	CXCR4 in SW480	Activation of transcription through STAT6 response element in immune cells (such as T-cells).
	1386	1387
	HOUCQ17	HOUDK26
	438	439

	routinely modified to test	sclerosis and/or as described
	STAT6 response element	below) and
	activity of the polypeptides of	immunodeficiencies (e.g., as
	the invention (including	described below).
	antibodies and agonists or	Preferred indications include
	antagonists of the invention)	neoplastic diseases (e.g.,
	include assays disclosed in	leukemia, lymphoma,
	Berger et al., Gene 66:1-10	melanoma, and/or as described
	(1998); Cullen and Malm,	below under
	Methods in Enzymol 216:362-	"Hyperproliferative
	368 (1992); Henthorn et al.,	Disorders"). Preferred
	Proc Natl Acad Sci USA	indications include neoplasms
	85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
	et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
	(1998); Moffatt et al.,	prostate, breast, lung, colon,
	Transplantation 69(7):1521-	pancreatic, esophageal,
	1523 (2000); Curiel et al., Eur	stomach, brain, liver and
	J Immunol 27(8):1982-1987	urinary cancer. Other preferred
	(1997); and Masuda et al., J	indications include benign
	Biol Chem 275(38):29331-	dysproliferative disorders and
	29337 (2000), the contents of	pre-neoplastic conditions, such
	each of which are herein	as, for example, hyperplasia,
	incorporated by reference in its	metaplasia, and/or dysplasia.
	entirety. T cells that may be	Preferred indications include
	used according to these assays	anemia, pancytopenia,
	are publicly available (e.g.,	leukopenia, thrombocytopenia,
	through the ATCC).	Hodgkin's disease, acute
	Exemplary T cells that may be	lymphocytic anemia (ALL),
	used according to these assays	plasmacytomas, multiple
	include the SUPT cell line,	myeloma, Burkitt's lymphoma,
	which is a suspension culture	arthritis, AIDS, granulomatous

				of IL-2 and IL-4 responsive T cells.	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious
440	HOVCA92	1388	IFNg in Human T- cell 2B9		
440	HOVCA92	1388	SEAP in NK16/STAT6		
440	HOVCA92	1388	SEAP in UMR-106		
441	HPASA81	1389	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced loF production and increases	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing)
				IgA production (IgA plays a role in mucosal immunity).  IL-6 induces cytotoxic T cells.  Deregulated expression of IL-6 has been linked to autoimmune	highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the etimulation or embancement

myelomas, and chronic	of mucosal immunity. Highly
 hyperproliferative diseases.	-
Assays for immunomodulatory	tory   blood disorders (e.g., as
and differentiation factor	
proteins produced by a large	
variety of cells where the	Related Disorders", and/or
 expression level is strongly	
regulated by cytokines, growth	wth and infection (e.g., as
 factors, and hormones are well	
known in the art and may be	e "Infectious Disease"). Highly
used or routinely modified to	to preferred indications include
assess the ability of	autoimmune diseases (e.g.,
polypeptides of the invention	on rheumatoid arthritis, systemic
(including antibodies and	-
agonists or antagonists of the	ne sclerosis and/or as described
invention) to mediate	below) and
immunomodulation and	immunodeficiencies (e.g., as
differentiation and modulate T	e T   described below). Highly
cell proliferation and function.	on. preferred indications also
Exemplary assays that test for	for include boosting a B cell-
immunomodulatory proteins	-
evaluate the production of	and alternatively suppressing a
cytokines, such as IL-6, and	
the stimulation and	response. Highly preferred
upregulation of T cell	indications include
proliferation and functional	inflammation and
activities. Such assays that	inflammatory
may be used or routinely	disorders. Additional highly
modified to test	preferred indications include
 immunomodulatory and	asthma and allergy. Highly
diffferentiation activity of	preferred indications include

	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma nlasmacytoma
	agonists or antagonists of the	leukemia, lymphoma.
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	when activated by antigen	leukopenia, thrombocytopenia,
	and/or cytokines, initiate and	Hodgkin's disease, acute
	upregulate T cell proliferation	lymphocytic anemia (ALL),
	and functional activities.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,

				suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious
HPBCU51	1390	Regulation of viability or proliferation of immune cells (such as human eosinophil EOL-1 cells).	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of eosinophil cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP	Highly preferred indications include eosinophilia, asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders.  Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), Highly preferred indications also include boosting or inhibiting

				present which signals the presence of metabolically active cells. Eosinophils are a type of immune cell important in allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Eosinophil cell lines that may be used according to these assays are publicly available and/or may be routinely generated. Exemplary eosinophil cells that may be used according to these assays include EOL-1 Cells.	immune cell proliferation. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include boosting an eosinophil-mediated immune response, and suppressing an eosinophil-mediated immune response.
442	HPBCU51	1390	Glucose Production in H4IIE		
442	HPBCU51	1390	SEAP in HIB/CRE		
442	HPBCU51	1390	Production of GM-CSF	GM-CSF FMAT. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytesmacrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally,	A highly preferred embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of GM-CSF. Highly preferred indications

GM-CSF plays an important	include inflammation and
role in the differentiation of	inflammatory disorders. An
dendritic cells and monocytes,	additional highly preferred
and increases antigen	indication is infection (e.g., as
presentation. GM-CSF is	described below under
considered to be a	"Infectious Disease".
proinflammatory cytokine.	Highly preferred indications
Assays for immunomodulatory	include blood disorders (e.g.,
proteins that promote the	neutropenia (and the
production of GM-CSF are	prevention of neutropenia
well known in the art and may	(e.g., in HIV infected patients),
be used or routinely modified	and/or as described below
 to assess the ability of	under "Immune Activity",
polypeptides of the invention	"Blood-Related Disorders",
(including antibodies and	and/or "Cardiovascular
agonists or antagonists of the	Disorders"). Highly preferred
invention) to mediate	indications also include
immunomodulation and	autoimmune diseases (e.g.,
modulate the growth and	rheumatoid arthritis, systemic
differentiation of leukocytes.	lupus erythematosis, multiple
Exemplary assays that test for	sclerosis and/or as described
immunomodulatory proteins	below) and
evaluate the production of	immunodeficiencies (e.g., as
cytokines, such as GM-CSF,	described below). Additional
and the activation of T cells.	highly preferred indications
Such assays that may be used	include asthma. Highly
or routinely modified to test	preferred indications include
immunomodulatory activity of	neoplastic diseases (e.g.,
polypeptides of the invention	leukemia (e.g., acute
(including antibodies and	lymphoblastic leukemia, and
agonists or antagonists of the	acute myelogenous leukemia),

			invention) include the assays	lymphoma (e.g., non-
			disclosed in Miraglia et al., J	Hodgkin"s lymphoma and
			Biomolecular Screening 4:193-	Hodgkin"s disease), and/or as
_			204 (1999); Rowland et al.,	described below under
	-		"Lymphocytes: a practical	"Hyperproliferative
	-		approach" Chapter 6:138-160	Disorders"). Highly preferred
			(2000); and Ye et al., J Leukoc	indications include neoplasms
-	_		Biol (58(2):225-233, the	and cancers, such as, leukemia,
-			contents of each of which are	lymphoma, melanoma, and
			herein incorporated by	prostate, breast, lung, colon,
			reference in its entirety.	pancreatic, esophageal,
	-		Natural killer cells that may be	stomach, brain, liver and
			used according to these assays	urinary cancer. Other preferred
			are publicly available (e.g.,	indications include benign
	_		through the ATCC) or may be	dysproliferative disorders and
	-		isolated using techniques	pre-neoplastic conditions, such
			disclosed herein or otherwise	as, for example, hyperplasia,
_			known in the art. Natural	metaplasia, and/or dysplasia.
			killer (NK) cells are large	Highly preferred indications
			granular lymphocytes that have	include: suppression of
			cytotoxic activity but do bind	immune reactions to
			antigen. NK cells show	transplanted organs and tissues
			antibody-independent killing	(e.g., bone marrow transplant);
			of tumor cells and also	accelerating myeloid recovery;
			recognize antibody bound on	and mobilizing hematopoietic
			target cells, via NK Fc	progenitor cells. Preferred
			receptors, leading to cell-	indications include boosting a
	_		mediated cytotoxicity.	T cell-mediated immune
				response, and alternatively,
				suppressing a T cell-mediated
				immune response. Preferred

					indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergy.
	HPBCU51	1390	IL-8 in SW480		
	HPBCU51	1390	SEAP in UMR-106		
	HPDDC77	1391	Activation of T-Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation,	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly

	activation, and apoptosis.	preferred indications include
	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other
	according to these assays are	preferred indications include
	publicly available (e.g.,	benign dysproliferative
	through the ATCC).	disorders and pre-neoplastic
	Exemplary mouse T cells that	conditions, such as, for
	may be used according to these	example, hyperplasia,
	assays include the CTLL cell	metaplasia, and/or dysplasia.
!	line, which is an IL-2	Preferred indications include

				dependent suspension-culture cell line with cytotoxic activity.	arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meninoitis, and I yme Disease
443	HPDDC77	1391	IL-2 in Human T cells		
443	HPDDC77	1391	Caspase (+paclitaxel) in SW480		
444	HPDWP28	1392	SEAP in HIB/CRE		
444	HPDWP28	1392	CD152 in Human T cells		
445	HPEAD48	1393	Activation of transcription through NFAT response element in immune cells (such as mast cells).	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and

and in discontinue of tennessing in the most of the internal	through the Nuclear Factor of Preferred indications also	 	known in the art and may be "Immune Activity", "Blood-	used or routinely modified to Related Disorders", and/or	assess the ability of "Cardiovascular Disorders").	polypeptides of the invention   Preferred indications include	(including antibodies and autoimmune diseases (e.g.,	agonists or antagonists of the   rheumatoid arthritis, systemic	invention) to regulate NFAT   lupus erythematosis, multiple	transcription factors and sclerosis and/or as described	modulate expression of genes   below) and	involved in immunodeficiencies (e.g., as	immunomodulatory functions.   described below). Preferred	Exemplary assays for indications include neoplastic	transcription through the diseases (e.g., leukemia,	NFAT response element that   lymphoma, melanoma,	may be used or routinely prostate, breast, lung, colon,	modified to test NFAT- pancreatic, esophageal,	response element activity of stomach, brain, liver, and	polypeptides of the invention   urinary tract cancers and/or as	(including antibodies and described below under	agonists or antagonists of the ''Hyperproliferative	invention) include assays Disorders"). Other preferred	ene	66:1-10 (1998); Cullen and dysproliferative disorders and	Malm, Methods in Enzymol   pre-neoplastic conditions, such	216:362-368 (1992); Henthorn as, for example, hyperplasia,	at al Dron Matt Anad Coi HCA material and/or diversis	_

31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line					et al., Int J Biochem Cell Biol	anemia, pancytopenia,
et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chen 270(27):16333- 16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCO.) Exemplary human mast cells that may be used according to these assays include the HMC- 1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  SEAP in Senescence Assay  HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 signaling pathway in HMC-1 resconce element in human mast cell line activation activation of the man mast cell line activation activation of the GATA-3 signaling pathway in HMC-1 hurough 6ATA-3 signaling pathway in HMC-1 hurough 4ATA-3 signaling pathw					31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
Hutchinson and McCloskey, J Biol Chem 270(27):16333- 16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety.  Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell cell line, which is an immature man and exhibits many characteristics of immature mast cells.  HPEAD48 1393 SEAP in Senescence Assay  HPEBE79 1394 Activation of immature mast cells.  This reporter assay measures transcription activation of the GATA-3 signaling pathway in HMC-1 resonance element in human mast cell line forman mast cell line forman mast cell line senones element.					et al., J Immunol	leukemias, Hodgkin's disease,
Hutchinson and McCloskey, J Biol Chem 270(27):1633- 16338 (1995), and Tumer et al., 1 Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC- 1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells. SEAP in SEAP in SEAP in SEAP in This reporter assay measures transcription This reporter assay measures through 6ATA-3 signaling pathway in HMC-1 servouge element in human mast reall line					165(12):7215-7223 (2000);	acute lymphocytic anemia
Biol Chem 270(27):1633- 16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC- 1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HPEAD48 1393 SEAP in SEAP in Senescence Assay This reporter assay measures transcription This reporter assay measures transcription activation of the GATA-3 through GATA-3 thr					Hutchinson and McCloskey, J	(ALL), plasmacytomas,
16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety.  Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  SEAP in  HPEAD48  SEAP in  Senescence Assay  This reporter assay measures transcription  This reporter assay measures transcription activities of the measures transcription ac					Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
al., J Exp Med 188:527-537  (1998), the contents of each of which are herein incorporated by reference in its entirety.  Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell line established from the peripheral blood of a patient with mast cell immature mast cells.  BEAP in  SEAP in  Senescence Assay  This reporter assay measures through GATA-3 signaling pathway in HMC-1 resonance element in human mast cell line human m					16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
(1998), the contents of each of which are herein incorporated by reference in its entirety.  Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell lendermin, and exhibits many characteristics of immature mast cells.  HPEAD48 1393 SEAP in Senescence Assay  HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 signaling pathway in HMC-1 human mast cell line human mast cell line human mast cell line human mast cells.					al., J Exp Med 188:527-537	granulomatous disease,
which are herein incorporated by reference in its entirety.  Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell line stablished from the peripheral blood of a patient with mast cell line assays include the HMC-1 less assays and according to the		-			(1998), the contents of each of	inflammatory bowel disease,
hy reference in its entirety.  Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HPEAD48 1393 SEAP in Senescence Assay  HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 through the day and the cell fine activation of the day activation of the man mast cell in the man mast cell in the center assay measures transcription activation of the GATA-3 signaling pathway in HMC-1 through GATA-3 through GATA-3 signaling pathway in HMC-1 through GATA-3 through GATA-3 signaling pathway in HMC-1 through GATA-3 through					which are herein incorporated	sepsis, neutropenia,
Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell line many characteristics of immature mast cells.  HPEAD48 1393 SEAP in Senescence Assay  HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 resonance element in human mast cell line					by reference in its entirety.	neutrophilia, psoriasis,
according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HPEAD48 1393 SEAP in Senescence Assay  HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 personne element in human mast cell line.					Mast cells that may be used	suppression of immune
hrough the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC- 1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 resonce element in human mast cell line					according to these assays are	reactions to transplanted
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of HPEAD48 signaling pathway in HMC-1 restronce element in human mast cell line restronce element in human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 signaling pathway in HMC-1 human mast cell line human mast cell line human mast cell line human mast cell line					publicly available (e.g.,	organs and tissues, hemophilia,
Exemplary human mast cells that may be used according to these assays include the HMC-    1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.    HPEAD48 1393 SEAP in Senescence Assay    HPEBE79 1394 Activation of This reporter assay measures transcription    transcription    transcription    signaling pathway in HMC-1 servonce element in human mast cell line human mast cell line human mast cell line					through the ATCC).	hypercoagulation, diabetes
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 tresponse element in human mast cell line established from the peripheral blood of a patient with mast cell line established from the peripheral blood of a patient with mast cell line activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 human mast cell line hum					Exemplary human mast cells	mellitus, endocarditis,
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription through GATA-3 signaling pathway in HMC-1 response element in human mast cell line.					that may be used according to	meningitis, and Lyme Disease.
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription through GATA-3 signaling pathway in HMC-1 transcription transcription through GATA-3 signaling pathway in HMC-1 transcription transc					these assays include the HMC-	
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 signaling pathway in HMC-1 resonne element in human mast cell line					1 cell line, which is an	
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in human mast cell line					immature human mast cell line	
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in human mast cell line					established from the peripheral	
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in human mast cell line					blood of a patient with mast	
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in human mast cell line					cell leukemia, and exhibits	
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in human mast cell line					many characteristics of	
HPEAD48 1393 SEAP in Senescence Assay HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in human mast cell line					immature mast cells.	
HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in human mast cell line		HPEAD48	1393	SEAP in		
HPEBE79 1394 Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in human mast cell line	445			Senescence Assay		
transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in human mast cell line		HPEBE79	1394	Activation of	This reporter assay measures	Highly preferred indications
signaling pathway in HMC-1	446			transcription	activation of the GATA-3	include allergy, asthma, and
human mast cell line			-	through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
Hailian mast con this.				response element in	human mast cell line.	indications include infection

	immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
	as mast cells).	cells has been linked to	described below under
		cytokine and chemokine	"Infectious Disease"), and
		production. Assays for the	inflammation and
		activation of transcription	inflammatory disorders.
-		through the GATA3 response	Preferred indications also
		element are well-known in the	include blood disorders (e.g.,
		art and may be used or	as described below under
		routinely modified to assess	"Immune Activity", "Blood-
		the ability of polypeptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
		antibodies and agonists or	Preferred indications include
		antagonists of the invention) to	autoimmune diseases (e.g.,
		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
		expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and

				et al Proc Natl Acad Sci USA	pre-neoplastic conditions, such
				85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
				Quant Biol 64:563-571 (1999);	Preferred indications include
				Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
				J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
		<del>-</del> -		herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				I cell line, which is an	meningitis, and Lyme Disease.
-				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
		_		immature mast cells.	
	HPFCL43	1395	SEAP in ATP-3T3-		
447			L1		
Ţ	HPFCL43	1395	Activation of	Assays for the activation of	A preferred embodiment of
44/			transcription	transcription through the	the invention includes a

through serum	Serum Response Element	method for inhibiting (e.g.,
response element in	(SRE) are well-known in the	reducing) TNF alpha
immune cells (such	art and may be used or	production. An alternative
as T-cells).	routinely modified to assess	preferred embodiment of the
	the ability of polypeptides of	invention includes a method
	the invention (including	for stimulating (e.g.,
	antibodies and agonists or	increasing) TNF alpha
	antagonists of the invention) to	production. Preferred
	regulate the serum response	indications include blood
	factors and modulate the	disorders (e.g., as described
	expression of genes involved	below under "Immune
	in growth. Exemplary assays	Activity", "Blood-Related
	for transcription through the	Disorders", and/or
	SRE that may be used or	"Cardiovascular Disorders"),
	routinely modified to test SRE	Highly preferred indications
	activity of the polypeptides of	include autoimmune diseases
	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
	antagonists of the invention)	Crohn"s disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
·	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid

					arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
447	HPFCL43	1395	Caspase (+camptothecin) in SW480		diad illications Discuss ).
448	HPFDG48	1396	SEAP in 293/ISRE		
448	HPFDG48	1396	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production.

	routinely modified to assess	Highly preferred indications
	the ability of polypeptides of	include blood disorders (e.g.,
	the invention (including	as described below under
	antibodies and agonists or	"Immune Activity", "Blood-
	antagonists of the invention) to	Related Disorders", and/or
	mediate immunomodulation,	"Cardiovascular Disorders"),
	modulate inflammation and	Highly preferred indications
	cytotoxicity. Exemplary	include autoimmune diseases
	assays that test for	(e.g., rheumatoid arthritis,
	immunomodulatory proteins	systemic lupus erythematosis,
	evaluate the production of	Crohn"s disease, multiple
	cytokines such as tumor	sclerosis and/or as described
	necrosis factor alpha (TNFa),	below), immunodeficiencies
	and the induction or inhibition	(e.g., as described below),
	of an inflammatory or	boosting a T cell-mediated
	cytotoxic response. Such	immune response, and
	assays that may be used or	suppressing a T cell-mediated
	routinely modified to test	immune response. Additional
	immunomodulatory activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders, and
	agonists or antagonists of the	treating joint damage in
	invention) include assays	patients with rheumatoid
	disclosed in Miraglia et al., J	arthritis. An additional highly
	Biomolecular Screening 4:193-	preferred indication is sepsis.
	204(1999); Rowland et al.,	Highly preferred indications
 	"Lymphocytes: a practical	include neoplastic diseases
 	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); Verhasselt et al., Eur J	and/or as described below
	Immunol 28(11):3886-3890	under "Hyperproliferative
	(1198); Dahlen et al., J	Disorders"). Additionally,

	Imminol 160/7):3585-3503	highly preferred indications
	CCC-COCC.(1)001 IOIIIIIII	inging prefered marganens
	(1998); Verhasselt et al., J	include neoplasms and
	Immunol 158:2919-2925	cancers, such as, leukemia,
	 (1997); and Nardelli et al., J	lymphoma, melanoma, glioma
	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
	(1999), the contents of each of	tumors, and prostate, breast,
	which are herein incorporated	lung, colon, pancreatic,
	by reference in its entirety.	esophageal, stomach, brain,
	Human dendritic cells that may	liver and urinary cancer. Other
	be used according to these	preferred indications include
	assays may be isolated using	benign dysproliferative
	techniques disclosed herein or	disorders and pre-neoplastic
	otherwise known in the art.	conditions, such as, for
	Human dendritic cells are	example, hyperplasia,
	antigen presenting cells in	metaplasia, and/or dysplasia.
	suspension culture, which,	Preferred indications include
	when activated by antigen	anemia, pancytopenia,
	and/or cytokines, initiate and	leukopenia, thrombocytopenia,
	upregulate T cell proliferation	Hodgkin's disease, acute
	and functional activities.	lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,

					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HPFDG48	1396	Activation of	Assays for the activation of	Highly preferred indications
448			transcription	transcription through the	include allergy, asthma, and
			through STAT6	Signal Transducers and	rhinitis. Additional highly
			response element in	Activators of Transcription	preferred indications include
			immune cells (such	(STAT6) response element in	infection (e.g., an infectious
			as mast cells).	immune cells (such as in the	disease as described below
				human HMC-1 mast cell line)	under "Infectious Disease"),
				are well-known in the art and	and inflammation and
				may be used or routinely	inflammatory disorders.
				modified to assess the ability	Preferred indications also
				of polypeptides of the	include hematopoietic and
				invention (including antibodies	immunological disorders (e.g.,
				and agonists or antagonists of	as described below under
		_		the invention) to regulate	"Immune Activity", "Blood-
				STAT6 transcription factors	Related Disorders", and/or
				and modulate the expression of	"Cardiovascular Disorders"),
				multiple genes. Exemplary	autoimmune diseases (e.g.,
		_		assays for transcription	rheumatoid arthritis, systemic
				through the STAT6 response	lupus erythematosis, multiple
				element that may be used or	sclerosis and/or as described
				routinely modified to test	below), and
				STAT6 response element	immunodeficiencies (e.g., as
				activity of the polypeptides of	described below). Preferred
				the invention (including	indications include neoplastic

antibodies and agonists or	diseases (e.g., leukemia,
antagonists of the invention)	lymphoma, melanoma, and/or
include assays disclosed in	as described below under
Berger et al., Gene 66:1-10	"Hyperproliferative
(1998); Cullen and Malm,	Disorders"). Preferred
Methods in Enzymol 216:362-	indications include neoplasms
368 (1992); Henthorn et al.,	and cancer, such as, for
 Proc Natl Acad Sci USA	example, leukemia, lymphoma,
85:6342-6346 (1988);	melanoma, and prostate,
Sherman, Immunol Rev	breast, lung, colon, pancreatic,
179:48-56 (2001); Malaviya	esophageal, stomach, brain,
and Uckun, J Immunol	liver and urinary cancer. Other
168:421-426 (2002); Masuda	preferred indications include
et al., J Biol Chem	benign dysproliferative
275(38):29331-29337 (2000);	disorders and pre-neoplastic
and Masuda et al., J Biol Chem	conditions, such as, for
276:26107-26113 (2001), the	example, hyperplasia,
 contents of each of which are	metaplasia, and/or dysplasia.
herein incorporated by	Preferred indications include
reference in its entirety. Mast	hematopoietic and
 cells that may be used	immunological disorders such
according to these assays are	as arthritis, AIDS,
publicly available (e.g.,	granulomatous disease,
through the ATCC).	inflammatory bowel disease,
Exemplary human mast cells	sepsis, neutropenia,
that may be used according to	neutrophilia, psoriasis,
these assays include the HMC-	suppression of immune
1 cell line, which is an	reactions to transplanted
immature human mast cell line	organs and tissues, hemophilia,
established from the peripheral	hypercoagulation, diabetes
blood of a patient with mast	mellitus, endocarditis,

					cell leukemia, and exhibits	meningitis, and Lyme Disease.
					many characteristics of immature mast cells.	!
4	448	HPFDG48	1396	SEAP in OE-21		
4	448	HPFDG48	1396	SEAP in UMR-106		
4	449	HPIAQ68	1397	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong	A highly preferred embodiment of the invention
					effects on B cells. IL-6	includes a method for
					participates in IL-4 induced	stimulating (e.g., increasing)
					IgE production and increases	IL-6 production. An alternative
					IgA production (IgA plays a	highly preferred embodiment
					role in mucosal immunity).	of the invention includes a
					IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
261					Deregulated expression of IL-6	reducing) IL-6 production. A
					has been linked to autoimmune	highly preferrred indication is
					disease, plasmacytomas,	the stimulation or enhancement
					myelomas, and chronic	of mucosal immunity. Highly
					hyperproliferative diseases.	preferred indications include
					Assays for immunomodulatory	blood disorders (e.g., as
					and differentiation factor	described below under
					proteins produced by a large	"Immune Activity", "Blood-
					variety of cells where the	Related Disorders", and/or
					expression level is strongly	"Cardiovascular Disorders"),
					regulated by cytokines, growth	and infection (e.g., as
					factors, and hormones are well	described below under
					known in the art and may be	"Infectious Disease"). Highly
					used or routinely modified to	preferred indications include
					assess the ability of	autoimmune diseases (e.g.,
					polypeptides of the invention	rheumatoid arthritis, systemic

	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
 	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
 	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
 	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,

				by reference in its entirety.	stomach, brain, liver and
				Human dendritic cells that may	urinary cancer. Other preferred
				be used according to these	indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
_					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
449	HPIAQ68	1397	Production of MCP-1	MCP-1 FMAT. Assays for imminomodulatory proteins	A highly preferred embodiment of the invention
\f-			1401 -1	minimization and proteins	Chicoament of the mychical

	that are produced by a large	y a large	includes a method for
_	variety of cells and act to	act to	stimulating (e.g., increasing)
	induce chemotaxis and	and	MCP-1 production. An
	activation of monocytes and T	ytes and T	alternative highly preferred
	cells are well known in the art	n in the art	embodiment of the invention
_	and may be used or routinely	routinely	includes a method for
	modified to assess the ability	he ability	inhibiting (e.g., reducing)
	of polypeptides of the	he	MCP-1 production. A highly
	invention (including antibodies	g antibodies	preferred indication is
	and agonists or antagonists of	gonists of	infection (e.g., an infectious
	the invention) to mediate	ediate	disease as described below
	immunomodulation, induce	, induce	under "Infectious Disease").
	chemotaxis, and modulate	dulate	Additional highly preferred
	immune cell activation.	ion.	indications include
	Exemplary assays that test for	hat test for	inflammation and
	immunomodulatory proteins	proteins	inflammatory disorders.
	evaluate the production of cell	tion of cell	Preferred indications include
-	surface markers, such as	ch as	blood disorders (e.g., as
	monocyte chemoattractant	ractant	described below under
	protein (MCP), and the	the	"Immune Activity", "Blood-
 _	activation of monocytes and T	ytes and T	Related Disorders", and/or
	cells. Such assays that may be	hat may be	"Cardiovascular Disorders").
	used or routinely modified to	odified to	Highly preferred indications
	test immunomodulatory and	ntory and	include autoimmune diseases
	diffferentiation activity of	vity of	(e.g., rheumatoid arthritis,
	polypeptides of the invention	invention	systemic lupus erythematosis,
	(including antibodies and	es and	multiple sclerosis and/or as
	agonists or antagonists of the	ists of the	described below) and
	invention) include assays	ıssays	immunodeficiencies (e.g., as
	disclosed in Miraglia et al., J	ia et al., J	described below). Preferred
	Biomolecular Screening 4:193-	ning 4:193-	indications also include

	204(1999); Rowland et al.,	anemia, pancytopenia,
	"Lymphocytes: a practical	leukopenia, thrombocytopenia,
	approach" Chapter 6:138-160	Hodgkin's disease, acute
 	(2000); Satthaporn and	lymphocytic anemia (ALL),
	Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
	45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
	Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
	158:2919-2925 (1997), the	disease, inflammatory bowel
	contents of each of which are	disease, sepsis, neutropenia,
 	herein incorporated by	neutrophilia, psoriasis,
	reference in its entirety.	suppression of immune
	Human dendritic cells that may	reactions to transplanted
	be used according to these	organs and tissues,
	assays may be isolated using	hemophilia, hypercoagulation,
	techniques disclosed herein or	diabetes mellitus, endocarditis,
 _	otherwise known in the art.	meningitis (bacterial and
	Human dendritic cells are	viral), Lyme Disease, asthma,
	antigen presenting cells in	and allergy Preferred
	suspension culture, which,	indications also include
	when activated by antigen	neoplastic diseases (e.g.,
	and/or cytokines, initiate and	leukemia, lymphoma, and/or as
	upregulate T cell proliferation	described below under
	and functional activities.	"Hyperproliferative
		Disorders"). Highly preferred
		indications include neoplasms
		and cancers, such as, leukemia,
		lymphoma, prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver, and urinary cancer. Other
		preferred indications include

					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HPIB015	1398	Regulation of	Assays for the regulation of	A highly preferred indication
450			viability and	viability and proliferation of	is diabetes mellitus. An
			proliferation of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
				the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
	-			antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
				regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
				cells. For example, the Cell	Disorders" section below),
				Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
				culture based on quantitation	neuropathy), blood vessel
				of the ATP present which	blockage, heart disease, stroke,
				signals the presence of	impotence (e.g., due to diabetic
				metabolically active cells.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test regulation of viability and	nonketotic hyperglycemic-
				proliferation of pancreatic beta	hyperosmolar coma,
·	-			cells by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,

			the invention) include assays	hypertension, stroke, and other
			disclosed in: Friedrichsen BN,	diseases and disorders as
			et al., Mol Endocrinol,	described in the
			15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
			MA, et al., Endocrinology,	section below), dyslipidemia,
			139(4):1494-9 (1998); Hugl	endocrine disorders (as
			SR, et al., J Biol Chem 1998	described in the "Endocrine
			Jul 10;273(28):17771-9	Disorders" section below),
			(1998), the contents of each of	neuropathy, vision impairment
			which is herein incorporated	(e.g., diabetic retinopathy and
			by reference in its entirety.	blindness), ulcers and impaired
			Pancreatic cells that may be	wound healing, and infection
			used according to these assays	(e.g., infectious diseases and
			are publicly available (e.g.,	disorders as described in the
			through the ATCC) and/or	"Infectious Diseases" section
			may be routinely generated.	below, especially of the
			Exemplary pancreatic cells that	urinary tract and skin), carpal
			may be used according to these	tunnel syndrome and
			assays include rat INS-1 cells.	Dupuytren's contracture). An
			INS-1 cells are a semi-	additional highly preferred
			adherent cell line established	indication is obesity and/or
			from cells isolated from an X-	complications associated with
			ray induced rat transplantable	obesity. Additional highly
			insulinoma. These cells retain	preferred indications include
			characteristics typical of native	weight loss or alternatively,
			pancreatic beta cells including	weight gain. Additional highly
			glucose inducible insulin	preferred indications are
			secretion. References: Asfari	complications associated with
			et al. Endocrinology 1992	insulin resistance.
			130:167.	
HPIB015	1398	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred

450	by T cells and has strong	embodiment of the invention
	 effects on B cells. IL-6	includes a method for
	participates in IL-4 induced	stimulating (e.g., increasing)
	IgE production and increases	
	IgA production (IgA plays a	highly preferred embodiment
	role in mucosal immunity).	of the invention includes a
	L-6 induces cytotoxic T cells.	ls. method for inhibiting (e.g.,
	Deregulated expression of IL-6	
	has been linked to autoimmune	
	disease, plasmacytomas,	the stimulation or enhancement
_	myelomas, and chronic	of mucosal immunity. Highly
	hyperproliferative diseases.	preferred indications include
	Assays for immunomodulatory	ory blood disorders (e.g., as
	and differentiation factor	
	proteins produced by a large	
	variety of cells where the	Related Disorders", and/or
	expression level is strongly	"Cardiovascular Disorders"),
	regulated by cytokines, growth	th and infection (e.g., as
	factors, and hormones are well	ell   described below under
	known in the art and may be	"Infectious Disease"). Highly
	used or routinely modified to	preferred indications include
	assess the ability of	autoimmune diseases (e.g.,
	polypeptides of the invention	n rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	s sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
_	differentiation and modulate T	T   described below). Highly
	cell proliferation and function.	n. preferred indications also
	Exemplary assays that test for	or include boosting a B cell-
	immunomodulatory proteins	mediated immune response

id t t t t t t t t t t t t t t t t t t t	fo, and  fo, and  fo, and  s that ely  nd  y of  y of  y of  y of  s of the ays et al., J  ng 4:193- et al., J  ng 4:193- et al., fical  138-160  It et al., J  225  f each of  rporated irety. s that may these d using  nere ar.	fional state ely had be so the ely had and and and and and and and ans et al., I had be so fit et al., I had be so firety.  It et al., J had be so firety.  It each of the act of sare had be so firety.
evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.	evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are	evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are

				suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infectiou (e.g., an infectious disease as described below under "Infectious
450	HPIBO15	1398	Glucose Production in H4IIE		Disease ).
451	HPICB53	1399	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell

invention) to promote caspase	growth. A highly preferred
 protease-mediated apoptosis.	ૃ
Induction of apoptosis in	includes a method for
endothelial cells supporting the	s stimulating endothelial cell
vasculature of tumors is	proliferation. An alternative
associated with tumor	highly preferred embodiment
regression due to loss of tumor	
blood supply. Exemplary	method for inhibiting
assays for caspase apoptosis	endothelial cell proliferation.
that may be used or routinely	A highly preferred
modified to test capase	embodiment of the invention
apoptosis activity of	includes a method for
polypeptides of the invention	stimulating apoptosis of
(including antibodies and	endothelial cells. An
agonists or antagonists of the	alternative highly preferred
invention) include the assays	embodiment of the invention
disclosed in Lee et al., FEBS	includes a method for
Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
209-218 (2000); and Karsan	A highly preferred
and Harlan, J Atheroscler	embodiment of the invention
Thromb 3(2): 75-80 (1996);	includes a method for
the contents of each of which	stimulating angiogenisis. An
are herein incorporated by	alternative highly preferred
reference in its entirety.	embodiment of the invention
Endothelial cells that may be	includes a method for
used according to these assays	inhibiting angiogenesis. A
are publicly available (e.g.,	highly preferred embodiment
through commercial sources).	of the invention includes a
Exemplary endothelial cells	method for reducing cardiac
that may be used according to	hypertrophy. An alternative

highly preferred embodiment	method for inducing cardiac	hypertrophy. Highly	S	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels
these assays include bovine	(hAFC) which are an evample	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																					
																							-						
																			-										

themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	Toront citoracaca	palicicalic, esopliageal,

	urinary cancer. Preferred
	indications include benion
	 descentification discondens and
	dyspionienanive disolders and
	pre-neoplastic conditions, such
 	as, for example, hyperplasia,
	metaplasia, and/or dysplasia.
	Highly preferred indications
 	also include arterial disease,
	such as, atherosclerosis,
	hypertension, coronary artery
	disease, inflammatory
	vasculitides, Reynaud"s
	disease and Reynaud"s
	phenomenom, aneurysms,
	restenosis; venous and
	lymphatic disorders such as
	thrombophlebitis,
	lymphangitis, and
 	lymphedema; and other
	vascular disorders such as
	peripheral vascular disease,
 	and cancer. Highly
	preferred indications also
	include trauma such as
	wounds, burns, and injured
	tissue (e.g., vascular injury
 	such as, injury resulting from
	balloon angioplasty, and
	atheroschlerotic lesions),
 	implant fixation, scarring,
	ischemia reperfusion injury,

					below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease
452	HPJBK12	1400	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polymentides of	and Crohn's disease), and pain management.  A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g.
				the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies.	diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuronathy, nervie
				pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes.  Exemplary assays that may be	disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental

	nse	used or routinely modified to	confusion, drowsiness,
	tesi	test for stimulation of insulin	nonketotic hyperglycemic-
	sec	secretion (from pancreatic	hyperosmolar coma,
	lea	cells) by polypeptides of the	cardiovascular disease (e.g.,
	vii	invention (including antibodies	heart disease, atherosclerosis,
	anc	and agonists or antagonists of	microvascular disease,
	the	the invention) include assays	hypertension, stroke, and other
	dis	disclosed in: Shimizu, H., et	diseases and disorders as
	al.,	al., Endocr J, 47(3):261-9	described in the
	(20	(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
	Mo	Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
	17	17 (1999); Filipsson, K., et al.,	endocrine disorders (as
	An	Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
	(19	(1998); Olson, L.K., et al., J	Disorders" section below),
	Bic	Biol Chem, 271(28):16544-52	neuropathy, vision impairment
	(19	(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
	oof	Journal of Biomolecular	blindness), ulcers and impaired
-	Scr	Screening, 4:193-204 (1999),	wound healing, and infection
	the	the contents of each of which	(e.g., infectious diseases and
 	is h	s herein incorporated by	disorders as described in the
	refe	reference in its entirety.	"Infectious Diseases" section
 -	Par	Pancreatic cells that may be	below, especially of the
	asn	used according to these assays	urinary tract and skin), carpal
_	are	are publicly available (e.g.,	tunnel syndrome and
	thre	through the ATCC) and/or	Dupuytren's contracture).
 	ma	may be routinely generated.	An additional highly preferred
	Exe	Exemplary pancreatic cells that	indication is obesity and/or
	ma	may be used according to these	complications associated with
	ass	assays include HITT15 Cells.	obesity. Additional highly
	H	HITT15 are an adherent	preferred indications include
	epi	epithelial cell line established	weight loss or alternatively,

				from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-177 Refs: Lord and	weight gain. Additional highly preferred indications are complications associated with insulin resistance.
452	HPJBK12	1400	Regulation of	Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981. Caspase Apoptosis. Assays for caspase anontosis are well	Preferred embodiments of the invention include using
1			immune cells (such as mast cells).	known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase	polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and
				protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E -	inflammation.

antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.	Immune cells that may be used	according to these assays are
		-																												

					publicly available (e.g.,	
					through commercial sources).	
					Exemplary immune cells that	
					may be used according to these	
	_				assays include mast cells such	
					as the HMC human mast cell	
					line.	
	H	HPJBK12	1400	Activation of	Kinase assay. JNK and p38	A highly preferred
452	<u>.</u>			Endothelial Cell	kinase assays for signal	embodiment of the invention
				p38 or JNK	transduction that regulate cell	includes a method for
				Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
					apoptosis are well known in	growth. An alternative highly
					the art and may be used or	preferred embodiment of the
					routinely modified to assess	invention includes a method
					the ability of polypeptides of	for inhibiting endothelial cell
26.					the invention (including	growth. A highly preferred
					antibodies and agonists or	embodiment of the invention
					antagonists of the invention) to	includes a method for
					promote or inhibit cell	stimulating endothelial cell
	_				proliferation, activation, and	proliferation. An alternative
					apoptosis. Exemplary assays	highly preferred embodiment
					for JNK and p38 kinase	of the invention includes a
					activity that may be used or	method for inhibiting
					routinely modified to test JNK	endothelial cell proliferation.
					and p38 kinase-induced	A highly preferred
					activity of polypeptides of the	embodiment of the invention
					invention (including antibodies	includes a method for
				-	and agonists or antagonists of	stimulating apoptosis of
					the invention) include the	endothelial cells. An
					assays disclosed in Forrer et	alternative highly preferred
					al., Biol Chem 379(8-9):1101-	embodiment of the invention

1110 (1998); Gupta et al., Exp	includes a method for
Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
Soc Symp 64:29-48 (1999);	A highly preferred
Chang and Karin, Nature	embodiment of the invention
410(6824):37-40 (2001); and	includes a method for
Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
the contents of each of which	alternative highly preferred
are herein incorporated by	embodiment of the invention
reference in its entirety.	includes a method for
Endothelial cells that may be	inhibiting (e.g., decreasing) the
used according to these assays	activation of and/or
are publicly available (e.g.,	inactivating endothelial cells.
through the ATCC).	A highly preferred
Exemplary endothelial cells	embodiment of the invention
that may be used according to	includes a method for
these assays include human	stimulating angiogenisis. An
umbilical vein endothelial cells	alternative highly preferred
(HUVEC), which are	embodiment of the invention
endothelial cells which line	includes a method for
venous blood vessels, and are	inhibiting angiogenesis. A
involved in functions that	highly preferred embodiment
include, but are not limited to,	of the invention includes a
angiogenesis, vascular	method for reducing cardiac
permeability, vascular tone,	hypertrophy. An alternative
and immune cell extravasation.	highly preferred embodiment
	of the invention includes a
	method for inducing cardiac
	hypertrophy. Highly
	preferred indications include

neoplastic diseases (e.g. as
described below under
"Hynernroliferative
Disorders") and disorders of
the cardiovascular system
(e.g., heart disease, congestive
heart failure, hypertension,
 aortic stenosis,
cardiomyopathy, valvular
regurgitation, left ventricular
dysfunction, atherosclerosis
 and atheroselerotic vascular
disease, diabetic nephropathy,
intracardiac shunt, cardiac
hypertrophy, myocardial
infarction, chronic
hemodynamic overload, and/or
as described below under
"Cardiovascular Disorders")
Highly preferred indications
include cardiovascular,
endothelial and/or angiogenic
disorders (e.g., systemic
disorders that affect vessels
such as diabetes mellitus, as
well as diseases of the vessels
themselves, such as of the
arteries, capillaries, veins
and/or lymphatics). Highly
preferred are indications that
stimulate angiogenesis and/or

		White Water Company
		calulovascularizationi. Linginiy
		preferred are indications that
		inhibit angiogenesis and/or
-		cardiovascularization.
		Highly preferred indications
		include antiangiogenic activity
		to treat solid tumors,
-		leukemias, and Kaposi"s
		sarcoma, and retinal disorders.
		Highly preferred indications
		include neoplasms and cancer,
		such as, Kaposi"s sarcoma,
		hemangioma (capillary and
		cavernous), glomus tumors,
		telangiectasia, bacillary
		angiomatosis,
		hemangioendothelioma,
		angiosarcoma,
		haemangiopericytoma,
		lymphangioma,
		lymphangiosarcoma. Highly
	***************************************	preferred indications also
		include cancers such as,
		prostate, breast, lung, colon,
		pancreatic, esophageal,
		stomach, brain, liver, and
		urinary cancer. Preferred
		indications include benign
		dysproliferative disorders and
		pre-neoplastic conditions, such
		as, for example, hyperplasia,

	metaplasia, and/or dysplasia.
	Highly preferred indications
	also include arterial disease,
-	such as, atherosclerosis,
	hypertension, coronary artery
	disease, inflammatory
	vasculitides, Reynaud"s
	disease and Reynaud"s
	phenomenom, aneurysms,
	restenosis; venous and
	lymphatic disorders such as
	thrombophlebitis,
	lymphangitis, and
	lymphedema; and other
	vascular disorders such as
	peripheral vascular disease,
	and cancer. Highly
	preferred indications also
	include trauma such as
	wounds, burns, and injured
	tissue (e.g., vascular injury
	such as, injury resulting from
	balloon angioplasty, and
	atheroschlerotic lesions),
	implant fixation, scarring,
	ischemia reperfusion injury,
	rheumatoid arthritis,
	cerebrovascular disease, renal
	diseases such as acute renal
	failure, and osteoporosis.
	A dditional binbly wastamad

indications include stroke.	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	nreferred indications include

					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
-					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HPJCL22	1401	Activation of	Kinase assay. Kinase assays,	A highly preferred
453			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
				inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
				test ERK kinase-induced	differentiation. A highly
				activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
				and agonists or antagonists of	for stimulating (e.g.,
-				the invention) include the	increasing) adipocyte
-				assays disclosed in Forrer et	activation. An alternative
				al., Biol Chem 379(8-9):1101-	highly preferred embodiment
				1110 (1998); Le Marchand-	of the invention includes a

Brustel Y. Exp Clin	method for inhibiting the
Endocrinol Diabetes	activation of (e.g., decreasing)
107(2):126-132 (1999);	and/or inactivating adipocytes.
Kyriakis JM, Biochem Soc	Highly preferred indications
Symp 64:29-48 (1999); Chang	include endocrine disorders
and Karin, Nature	(e.g., as described below under
410(6824):37-40 (2001); and	"Endocrine Disorders").
Cobb MH, Prog Biophys Mol	Highly preferred indications
Biol 71(3-4):479-500 (1999);	also include neoplastic
the contents of each of which	diseases (e.g., lipomas,
are herein incorporated by	liposarcomas, and/or as
 reference in its entirety.	described below under
Mouse adipocyte cells that	"Hyperproliferative
may be used according to these	Disorders"). Preferred
assays are publicly available	indications include blood
(e.g., through the ATCC).	disorders (e.g., hypertension,
Exemplary mouse adipocyte	congestive heart failure, blood
cells that may be used	vessel blockage, heart disease,
according to these assays	stroke, impotence and/or as
include 3T3-L1 cells. 3T3-L1	described below under
is an adherent mouse	"Immune Activity",
preadipocyte cell line that is a	"Cardiovascular Disorders",
 continuous substrain of 3T3	and/or "Blood-Related
fibroblast cells developed	Disorders"), immune disorders
through clonal isolation and	(e.g., as described below under
undergo a pre-adipocyte to	"Immune Activity"), neural
adipose-like conversion under	disorders (e.g., as described
appropriate differentiation	below under "Neural Activity
conditions known in the art.	and Neurological Diseases"),
	and infection (e.g., as
	described below under

"Infectious Disease"). A highly preferred indication is diabetes mellitus. An	additional highly preferred indication is a complication associated with diabetes (e.g.,	diabetic retinopathy, diabetic nephropathy, kidney disease	(e.g., renal failure, nephropathy and/or other	diseases and disorders as described in the "Renal	Disorders" section below), diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"
												-								

section below), dyslipidemia,
described in the "Endocrine
Disorders" section below),
neuropathy, vision impairment
(e.g., diabetic retinopathy and
blindness), ulcers and impaired wound healing infection (e.g.
 infectious diseases and
disorders as described in the
"Infectious Diseases" section
below (particularly of the
urinary tract and skin).
 additional highly preferred
indication is obesity and/or
 complications associated with
 obesity. Additional highly
preferred indications include
weight loss or alternatively,
weight gain.
 highly preferred indications are
complications associated with
insulin resistance.
Additional highly preferred
indications are disorders of the
musculoskeletal systems
including myopathies,
muscular dystrophy, and/or as
described herein.
 Additional highly preferred
 indications include,

					disease, dyslipidemia,
					gallstones, osteoarthritis,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
					indications include neoplasms
					and cancer, such as,
					lymphoma, leukemia and
					breast, colon, and kidney
					cancer. Additional preferred
					indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
-					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
453	HPJCL22	1401	CD152 in Human T		
	HPJCL22	1401	IL-8 in Normal		
453			Human Bronchial		
			Epitheliae		
	HPJCW04	1402	Production of TNF	TNFa FMAT. Assays for	A highly preferred
454			alpha by dendritic	immunomodulatory proteins	embodiment of the invention

cells	produced by activated	includes a method for
	macrophages, T cells,	inhibiting (e.g., decreasing)
	fibroblasts, smooth muscle,	TNF alpha production. An
	and other cell types that exert a	alternative highly preferred
	wide variety of inflammatory	embodiment of the invention
	and cytotoxic effects on a	includes a method for
	variety of cells are well known	stimulating (e.g., increasing)
	in the art and may be used or	TNF alpha production.
 	routinely modified to assess	Highly preferred indications
	the ability of polypeptides of	include blood disorders (e.g.,
	the invention (including	as described below under
	antibodies and agonists or	"Immune Activity", "Blood-
	antagonists of the invention) to	Related Disorders", and/or
	mediate immunomodulation,	"Cardiovascular Disorders"),
	modulate inflammation and	Highly preferred indications
	cytotoxicity. Exemplary	include autoimmune diseases
	assays that test for	(e.g., rheumatoid arthritis,
-	immunomodulatory proteins	systemic lupus erythematosis,
	evaluate the production of	Crohn"s disease, multiple
	cytokines such as tumor	sclerosis and/or as described
	necrosis factor alpha (TNFa),	below), immunodeficiencies
	and the induction or inhibition	(e.g., as described below),
	of an inflammatory or	boosting a T cell-mediated
	cytotoxic response. Such	immune response, and
	assays that may be used or	suppressing a T cell-mediated
	routinely modified to test	immune response. Additional
	immunomodulatory activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders, and
	agonists or antagonists of the	treating joint damage in
	invention) include assays	patients with rheumatoid

		disclosed in Miraglia et al J	arthritis. An additional highly
		Biomolecular Screening 4:193-	preferred indication is sepsis.
		204(1999); Rowland et al.,	Highly preferred indications
		"Lymphocytes: a practical	include neoplastic diseases
		approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
		(2000); Verhasselt et al., Eur J	and/or as described below
		Immunol 28(11):3886-3890	under "Hyperproliferative
		(1198); Dahlen et al., J	Disorders"). Additionally,
		Immunol 160(7):3585-3593	highly preferred indications
		(1998); Verhasselt et al., J	include neoplasms and
		Immunol 158:2919-2925	cancers, such as, leukemia,
		(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
		Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
		(1999), the contents of each of	tumors, and prostate, breast,
		which are herein incorporated	lung, colon, pancreatic,
		by reference in its entirety.	esophageal, stomach, brain,
		Human dendritic cells that may	liver and urinary cancer. Other
		be used according to these	preferred indications include
		assays may be isolated using	benign dysproliferative
		techniques disclosed herein or	disorders and pre-neoplastic
		otherwise known in the art.	conditions, such as, for
		Human dendritic cells are	example, hyperplasia,
		antigen presenting cells in	metaplasia, and/or dysplasia.
		suspension culture, which,	Preferred indications include
		when activated by antigen	anemia, pancytopenia,
-	,	and/or cytokines, initiate and	leukopenia, thrombocytopenia,
		upregulate T cell proliferation	Hodgkin's disease, acute
		and functional activities.	lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous

					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
	···				is infection (e.g., an infectious
					disease as described below
	!		,		under "Infectious Disease").
	HPJCW04	1402	SEAP in OE-21		
454					
	HPJEX20	1403	SEAP in		
455			NK16/STAT6		
	HPMAI22	1404	Activation of	Assays for the activation of	A highly preferred indication
456			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
			-	agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic

	expression of genes involved	nephropathy, kidney disease
	in a wide variety of cell	(e.g., renal failure,
 	functions. For example, a	nephropathy and/or other
	3T3-L1/CRE reporter assay	diseases and disorders as
	may be used to identify factors	described in the "Renal
-	that activate the cAMP	Disorders" section below),
	signaling pathway. CREB	diabetic neuropathy, nerve
	plays a major role in	disease and nerve damage
	adipogenesis, and is involved	(e.g., due to diabetic
	in differentiation into	neuropathy), blood vessel
	adipocytes. CRE contains the	blockage, heart disease, stroke,
	binding sequence for the	impotence (e.g., due to diabetic
	transcription factor CREB	neuropathy or blood vessel
	(CRE binding protein).	blockage), seizures, mental
	Exemplary assays for	confusion, drowsiness,
	transcription through the	nonketotic hyperglycemic-
	cAMP response element that	hyperosmolar coma,
	may be used or routinely	cardiovascular disease (e.g.,
	modified to test cAMP-	heart disease, atherosclerosis,
	response element activity of	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in Berger et al., Gene	section below), dyslipidemia,
	66:1-10 (1998); Cullen and	endocrine disorders (as
	Malm, Methods in Enzymol	described in the "Endocrine
	216:362-368 (1992); Henthorn	Disorders" section below),
	et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
	et al., Mol Cell Biol	blindness), ulcers and impaired

			20(3):1008-1020 (2000); and	wound healing, and infection
			Klemm et al., J Biol Chem	(e.g., infectious diseases and
			contents of each of which are	"Infectious Diseases" section
			herein incorporated by	below, especially of the
			reference in its entirety. Pre-	urinary tract and skin), carpal
			adipocytes that may be used	tunnel syndrome and
			according to these assays are	Dupuytren's contracture).
			publicly available (e.g.,	Additional highly preferred
			through the ATCC) and/or	indications are complications
			may be routinely generated.	associated with insulin
			Exemplary mouse adipocyte	resistance.
			cells that may be used	
			according to these assays	
			include 3T3-L1 cells. 3T3-L1	
			is an adherent mouse	
			preadipocyte cell line that is a	
			continuous substrain of 3T3	
			fibroblast cells developed	
			through clonal isolation and	
			undergo a pre-adipocyte to	
			adipose-like conversion under	
			appropriate differentiation	
	!		conditions known in the art.	
HPMAI22	1404	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include inflammation and
		through NFKB	NFKB response element are	inflammatory disorders.
		response element in	well-known in the art and may	Highly preferred indications
		immune cells (such	be used or routinely modified	include blood disorders (e.g.,
		as T-cells).	to assess the ability of	as described below under
			polypeptides of the invention	"Immune Activity", "Blood-

(including antibodies and	Related Disorders", and/or
agonists or antagonists of the	"Cardiovascular Disorders").
invention) to regulate NFKB	Highly preferred indications
transcription factors and	include autoimmune diseases
modulate expression of	(e.g., rheumatoid arthritis,
immunomodulatory genes.	systemic lupus erythematosis,
Exemplary assays for	multiple sclerosis and/or as
transcription through the	described below), and
NFKB response element that	immunodeficiencies (e.g., as
may be used or rountinely	described below). An
modified to test NFKB-	additional highly preferred
response element activity of	indication is infection (e.g.,
polypeptides of the invention	AIDS, and/or an infectious
(including antibodies and	disease as described below
agonists or antagonists of the	under "Infectious Disease").
invention) include assays	Highly preferred indications
disclosed in Berger et al., Gene	include neoplastic diseases
66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
Malm, Methods in Enzymol	lymphoma, and/or as described
216:362-368 (1992); Henthorn	below under
et al., Proc Natl Acad Sci USA	"Hyperproliferative
85:6342-6346 (1988); Black et	Disorders"). Highly preferred
al., Virus Gnes 15(2):105-117	indications include neoplasms
 (1997); and Fraser et al.,	and cancers, such as, for
29(3):838-844 (1999), the	example, melanoma, renal cell
contents of each of which are	carcinoma, leukemia,
herein incorporated by	lymphoma, and prostate,
reference in its entirety.	breast, lung, colon, pancreatic,
Exemplary human T cells,	esophageal, stomach, brain,
such as the MOLT4, that may	liver and urinary cancer. Other
be used according to these	preferred indications include

				assays are publicly available (e.g., through the ATCC).	benign dysproliferative disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications also
					include anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HPMFP40	1405	Activation of	Assays for the activation of	A preferred embodiment of
457			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha

antagonists of the invention) to	production. Preferred
 regulate the serum response	indications include blood
factors and modulate the	disorders (e.g., as described
expression of genes involved	below under "Immune
 in growth. Exemplary assays	Activity", "Blood-Related
for transcription through the	Disorders", and/or
SRE that may be used or	"Cardiovascular Disorders"),
 routinely modified to test SRE	Highly preferred indications
activity of the polypeptides of	include autoimmune diseases
the invention (including	(e.g., rheumatoid arthritis,
antibodies and agonists or	systemic lupus erythematosis,
antagonists of the invention)	Crohn's disease, multiple
include assays disclosed in	sclerosis and/or as described
 Berger et al., Gene 66:1-10	below), immunodeficiencies
(1998); Cullen and Malm,	(e.g., as described below),
Methods in Enzymol 216:362-	boosting a T cell-mediated
368 (1992); Henthorn et al.,	immune response, and
Proc Natl Acad Sci USA	suppressing a T cell-mediated
85:6342-6346 (1988); and	immune response. Additional
Black et al., Virus Genes	highly preferred indications
12(2):105-117 (1997), the	include inflammation and
content of each of which are	inflammatory disorders, and
herein incorporated by	treating joint damage in
reference in its entirety. T	patients with rheumatoid
cells that may be used	arthritis. An additional highly
according to these assays are	preferred indication is sepsis.
publicly available (e.g.,	Highly preferred indications
through the ATCC).	include neoplastic diseases
Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
may be used according to these	and/or as described below
assays include the CTLL cell	under "Hyperproliferative

Disorders"). Additionally, highly preferred indications include neoplasms and	cancers, such as, for example, leukemia. lymphoma.	melanoma, glioma (e.g., malignant glioma), solid	tumors, and prostate, breast,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and fissues
line, which is an IL-2 dependent suspension culture of T cells with cytotoxic	activity.																							
														-										
																			_					

					hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
458	HPMGJ45	1406	CD152 in Human T cells		
459	HPQAC69	1407	SEAP in 3T3L1		
459	HPQAC69	1407	CD152 in Human T cells		
460	HPRBC80	1408	SEAP in HIB/CRE		
460	HPRBC80	1408	Activation of transcription through GATA-3	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred
			response element in immune cells (such	human mast cell line. Activation of GATA-3 in mast	indications include infection (e.g., an infectious disease as
			as mast cells).	cells has been linked to cytokine and chemokine	described below under "Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription through the GATA3 response	inflammatory disorders. Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or

	the invention (including	"Cardiovascular Disorders").
	antibodies and agonists or	Preferred indications include
	antagonists of the invention) to	autoimmune diseases (e.g.,
	regulate GATA3 transcription	rheumatoid arthritis, systemic
	factors and modulate	lupus erythematosis, multiple
-	expression of mast cell genes	sclerosis and/or as described
	important for immune response	below) and
	development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
	element that may be used or	diseases (e.g., leukemia,
	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
 	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
	the invention) include assays	described below under
 	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred
	Malm, Methods in Enzymol	indications include benign
	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
 	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Quant Biol 64:563-571 (1999);	Preferred indications include
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
	Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's

				contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).	lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia,
·				that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
460	HPRBC80	1408	Activation of transcription through NFAT response element in immune cells (such as mast cells).	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-

	ass	assess the ability of	"Cardiovascular Disorders").
	lod	polypeptides of the invention	Preferred indications include
	ine	(including antibodies and	autoimmune diseases (e.g.,
	ago	agonists or antagonists of the	rheumatoid arthritis, systemic
	vni	invention) to regulate NFAT	lupus erythematosis, multiple
	trai	transcription factors and	sclerosis and/or as described
	om	modulate expression of genes	below) and
	vni	involved in	immunodeficiencies (e.g., as
	ımi	immunomodulatory functions.	described below). Preferred
	Exe	Exemplary assays for	indications include neoplastic
	trai	transcription through the	diseases (e.g., leukemia,
	HZ	NFAT response element that	lymphoma, melanoma,
	ma	may be used or routinely	prostate, breast, lung, colon,
	om	modified to test NFAT-	pancreatic, esophageal,
	res	response element activity of	stomach, brain, liver, and
	lod	polypeptides of the invention	urinary tract cancers and/or as
	(inc	(including antibodies and	described below under
	ago	agonists or antagonists of the	"Hyperproliferative
	vai	invention) include assays	Disorders"). Other preferred
	disc	disclosed in Berger et al., Gene	indications include benign
	:99	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Ma	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et a	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
-	85:	85:6342-6346 (1988); De Boer	Preferred indications include
	et a	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et a	et al., J Immunol	leukemias, Hodgkin's disease,
	165	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hu	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Bic	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's

				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HPRBC80	1408	Activation of	Assays for the activation of	Highly preferred indications
460			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
-			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),

	modulate expression of genes	immunodeficiencies (e.g., as
	involved in	described below), boosting a T
	immunomodulatory functions.	cell-mediated immune
	Exemplary assays for	response, and suppressing a T
	transcription through the	cell-mediated immune
	NFAT response element that	response. Additional highly
	may be used or routinely	preferred indications include
	modified to test NFAT-	inflammation and
	response element activity of	inflammatory disorders. An
	polypeptides of the invention	additional highly preferred
	(including antibodies and	indication is infection (e.g., an
	agonists or antagonists of the	infectious disease as described
	invention) include assays	below under "Infectious
	disclosed in Berger et al., Gene	Disease"). Preferred
-	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988);	"Hyperproliferative
	Aramburu et al., J Exp Med	Disorders"). Preferred
	182(3):801-810 (1995); De	indications include neoplasms
	Boer et al., Int J Biochem Cell	and cancers, such as, for
	Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. NK	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,

				according to these assays are	metaplasia, and/or dysplasia.
				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human NK cells	leukopenia, thrombocytopenia,
				that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HPRBC80	1408	Activation of	Assays for the activation of	A preferred embodiment of
460			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described

	p		rs"),	ons	ases	s,	tosis,	0)	peq	cies	<i>~</i> ;	pa		liated	itional	suc	q	and			ighly	psis.	ons	es	na,	×	e	у,	suc	
ımune	d-Relate	or	Disorde	l indicati	une dise	arthriti	rythema	multiple	as descri	deficien	ed below	l-mediate	e, and	cell-med	e. Addi	indication	ation an	sorders,	nage in	umatoid	litional }	ion is se	l indicati	ic diseas	lymphor	ed belor	oliferativ	ditional	indication	-
below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	-
below u	Activity	Disorde	"Cardio	Highly	include	(e.g., rh	systemi	Crohn"s	sclerosi	below),	(e.g., as	boostin	immune	suppres	immune	highly l	include	inflamu	treating	patients	arthritis	preferre	Highly	include	(e.g., le	and/or	" nnder	Disorde	highly l	
olved	e the	ed	Š.		e SRE	tinely	tivity	e Je	ibodies	ists of	ssays	l., Gene	and	/mol	enthorn	ci USA	Senson	:3862-	et al.,	117	ach of	orated	ety. T		's are			may be	assays	-
enes inv	ıpregulat	wth-rela	cell type	ys for	rough th	ed or rou	t SRE ac	ides of th	uding ant	antagon	nclude a	rger et a	; Cullen	s in Enzy	992); He	Acad S	(1988); E	ol 153(9)	nd Black	(2):105-	tent of ea	in incorp	its entire	e used	ese assay	ble (e.g.,	CC).	ells that	to these	11. T/T
expression of genes involved	in growth and upregulate the	function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	
expres	in grov	functic	genes	Exemp	transcr	that ma	modifi	of the	inventi	and ag	the inv	disclos	66:1-1	Malm,	216:36	et al., I	85:634	et al., J	3873 (	Virus (	(1997)	which	by refe	cells th	accord	public	throug	Exemp	used a	1.10
				_												_														
										•																	_	<u></u>		
							_				<del></del>			<del></del>							-		_							

≥ 2 C)	which is a human natural killer   cancers such as for example			 tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	
	whi	cell	cyte																											
			-																											

					cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
460	HPRBC80	1408	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and
				216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	inflammatory disorders. Highly preferred indications

85:6342-6346 (1988):	also include neoplastic
Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
272(49):30806-30811 (1997);	lymphoma, and/or as described
Chang et al., Mol Cell Biol	below under
18(9):4986-4993 (1998); and	"Hyperproliferative
Fraser et al., Eur J Immunol	Disorders"). Highly preferred
29(3):838-844 (1999), the	indications include neoplasms
contents of each of which are	and cancers, such as, leukemia,
herein incorporated by	lymphoma, prostate, breast,
reference in its entirety.	lung, colon, pancreatic,
Human T cells that may be	esophageal, stomach, brain,
used according to these assays	liver, and urinary cancer. Other
are publicly available (e.g.,	preferred indications include
through the ATCC).	benign dysproliferative
Exemplary human T cells that	disorders and pre-neoplastic
may be used according to these	conditions, such as, for
assays include the SUPT cell	example, hyperplasia,
line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
responsive suspension-culture	Preferred indications include
cell line.	arthritis, asthma, AIDS,
	allergy, anemia, pancytopenia,
	leukopenia, thrombocytopenia,
	Hodgkin's disease, acute
	lymphocytic anemia (ALL),
	plasmacytomas, multiple
	myeloma, Burkitt's lymphoma,
	granulomatous disease,
	inflammatory bowel disease,
	sepsis, psoriasis, suppression of
	immune reactions to
	transplanted organs and

					tissues, endocarditis, meningitis, and Lyme Disease.
160	HPRBC80	1408	Activation of	Assays for the activation of	Highly preferred indications
00			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as T-cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described
				invention) include assays	below under "Infectious
				disclosed in Berger et al., Gene	Disease"). Preferred
				66:1-10 (1998); Cullen and	indications include neoplastic
					diseases (e.g., leukemia,
				216:362-368 (1992); Henthorn	lymphoma, and/or as described

		et al Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988): Serfling	"Hynerproliferative
-		et al., Biochim Biophys Acta	Disorders"). Preferred
		1498(1):1-18 (2000); De Boer	indications include neoplasms
		et al., Int J Biochem Cell Biol	and cancers, such as, for
		31(10):1221-1236 (1999);	example, leukemia, lymphoma,
		Fraser et al., Eur J Immunol	and prostate, breast, lung,
		29(3):838-844 (1999); and	colon, pancreatic, esophageal,
		Yeseen et al., J Biol Chem	stomach, brain, liver and
		268(19):14285-14293 (1993),	urinary cancer. Other preferred
		the contents of each of which	indications include benign
		are herein incorporated by	dysproliferative disorders and
		reference in its entirety. T	pre-neoplastic conditions, such
		cells that may be used	as, for example, hyperplasia,
		according to these assays are	metaplasia, and/or dysplasia.
		publicly available (e.g.,	Preferred indications also
		through the ATCC).	include anemia, pancytopenia,
		Exemplary human T cells that	leukopenia, thrombocytopenia,
		may be used according to these	Hodgkin's disease, acute
		assays include the SUPT cell	lymphocytic anemia (ALL),
		line, which is a suspension	plasmacytomas, multiple
		culture of IL-2 and IL-4	myeloma, Burkitt's lymphoma,
		responsive T cells.	arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, sepsis, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,

					meningitis, Lyme Disease,
					asthma and allergy.
	HPRBC80	1408	Activation of	Assays for the activation of	Highly preferred indications
460			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative
				85:6342-6346 (1988); Black et	Disorders"). Highly preferred

	al., Virus Gnes 15(2):105-117	indications include neoplasms
	(1997); and Fraser et al.,	and cancers, such
	29(3):838-844 (1999), the	as,melanoma, renal cell
	contents of each of which are	carcinoma, leukemia,
	herein incorporated by	lymphoma, and prostate,
	reference in its entirety. T	breast, lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,
-	according to these assays are	liver and urinary cancer. Other
	publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	line, which is a suspension	metaplasia, and/or dysplasia.
	culture of IL-2 and IL-4	Preferred indications also
	responsive T cells.	include anemia, pancytopenia,
_		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS,
 		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, Lyme Disease,
		suppression of immune
		reactions to transplanted

					organs, asthma and allergy.
	HPRBF19	1409	Activation of	Assays for the activation of	Preferred embodiments of the
461			transcription	transcription through the	invention include using
			through NFKB	NFKB response element are	polypeptides of the invention
			response element in	well-known in the art and may	(or antibodies, agonists, or
			neuronal cells (such	be used or routinely modified	antagonists thereof) in
			as SKNMC cells).	to assess the ability of	detection, diagnosis,
				polypeptides of the invention	prevention, and/or treatment of
				(including antibodies and	Neurological Diseases and
				agonists or antagonists of the	Disorders (e.g. Alzheimer"s
				invention) to regulate NFKB	Disease, Parkinson"s Disease,
				transcription factors and	Brain Cancer, Seizures).
				modulate expression of	
				neuronal genes. Exemplary	
				assays for transcription	
				through the NFKB response	
			-	element that may be used or	
				routinely modified to test	
				NFKB-response element	
				activity of polypeptides of the	
				invention (including antibodies	
				and agonists or antagonists of	
				the invention) include assays	
	· -			disclosed in: Gill JS, et al.,	
				Neurobiol Dis, 7(4):448-461	
				(2000); Tamatani M, et al., J	
				Biol Chem, 274(13):8531-	
				8538 (1999); Berger et al.,	
				Gene 66:1-10 (1998); Cullen	
				and Malm, Methods in	
				Enzymol 216:362-368 (1992);	

	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell
Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary neuronal cells that may be used according to these assays include the SKNMC neuronal cell line.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the
	Endothelial Cell Apoptosis
	1410
	HPTTG19
	462

	vasculature of tumors is	proliferation. An alternative
	associated with tumor	highly preferred embodiment
	regression due to loss of tumor	of the invention includes a
	blood supply. Exemplary	method for inhibiting
	assays for caspase apoptosis	endothelial cell proliferation.
	that may be used or routinely	A highly preferred
	modified to test capase	embodiment of the invention
-	apoptosis activity of	includes a method for
	polypeptides of the invention	stimulating apoptosis of
	(including antibodies and	endothelial cells. An
	agonists or antagonists of the	alternative highly preferred
	invention) include the assays	embodiment of the invention
	disclosed in Lee et al., FEBS	includes a method for
	Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
	Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
	209-218 (2000); and Karsan	A highly preferred
	and Harlan, J Atheroscler	embodiment of the invention
	Thromb 3(2): 75-80 (1996);	includes a method for
	the contents of each of which	stimulating angiogenisis. An
	are herein incorporated by	alternative highly preferred
	reference in its entirety.	embodiment of the invention
	Endothelial cells that may be	includes a method for
	used according to these assays	inhibiting angiogenesis. A
	are publicly available (e.g.,	highly preferred embodiment
	through commercial sources).	of the invention includes a
	Exemplary endothelial cells	method for reducing cardiac
	that may be used according to	hypertrophy. An alternative
	these assays include bovine	highly preferred embodiment
	aortic endothelial cells	of the invention includes a
	(bAEC), which are an example	method for inducing cardiac
	of endothelial cells which line	hypertrophy. Highly

<u> </u>					(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	1
blood vessels and are involved in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																									
													_			-													

	stimulate angiogenesis and/or
	cardiovascularization. Highly
	preferred are indications that
	inhibit angiogenesis and/or
-	cardiovascularization.
	Highly preferred indications
	include antiangiogenic activity
-	to treat solid tumors,
	leukemias, and Kaposi"s
	sarcoma, and retinal disorders.
	Highly preferred indications
	include neoplasms and cancer,
	such as, Kaposi"s sarcoma,
	hemangioma (capillary and
 	cavernous), glomus tumors,
	telangiectasia, bacillary
	angiomatosis,
	hemangioendothelioma,
	angiosarcoma,
	haemangiopericytoma,
	lymphangioma,
	lymphangiosarcoma. Highly
	preferred indications also
	include cancers such as,
	prostate, breast, lung, colon,
	pancreatic, esophageal,
	stomach, brain, liver, and
	urinary cancer. Preferred
	indications include benign
	dysproliferative disorders and
	pre-neoplastic conditions, such

	metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s
	Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s
	also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s
	such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s
	hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s
	disease, inflammatory   vasculitides, Reynaud"s
	vasculitides, Reynaud"s
	disease and Reynaud"s
	phenomenom, aneurysms,
	restenosis; venous and
	lymphatic disorders such as
_	thrombophlebitis,
	lymphangitis, and
	lymphedema; and other
	vascular disorders such as
	peripheral vascular disease,
	and cancer. Highly
	preferred indications also
	include trauma such as
	wounds, burns, and injured
	tissue (e.g., vascular injury
	such as, injury resulting from
	balloon angioplasty, and
	atheroschlerotic lesions),
	implant fixation, scarring,
	ischemia reperfusion injury,
	rheumatoid arthritis,
	cerebrovascular disease, renal
	diseases such as acute renal
	failure, and osteoporosis.

					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
	O CARL ROLL OF				management.
463	HPTVX32	1411	SEAP in BEAS/NFkB		
	HPTVX32	1411	Activation of	This reporter assay measures	Highly preferred indications
463			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
_				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as

assays	assays for transcription	described below). Preferred
through	through the GATA3 response	indications include neoplastic
eleme	element that may be used or	diseases (e.g., leukemia,
routin	routinely modified to test	lymphoma, melanoma,
GAT/	GATA3-response element	prostate, breast, lung, colon,
activi	activity of polypeptides of the	pancreatic, esophageal,
invent	invention (including antibodies	stomach, brain, liver, and
and ag	and agonists or antagonists of	urinary tract cancers and/or as
the in.	the invention) include assays	described below under
disclo	disclosed in Berger et al., Gene	"Hyperproliferative
[-1:99]	66:1-10 (1998); Cullen and	Disorders"). Other preferred
Malm	Malm, Methods in Enzymol	indications include benign
216:3	216:362-368 (1992); Henthorn	dysproliferative disorders and
et al.,	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
85:63	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al.,	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant	Quant Biol 64:563-571 (1999);	Preferred indications include
Rodri	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Imm	I Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999)	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 8	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
Hende	Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
14(6):	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
conter	contents of each of which are	lymphoma, arthritis, AIDS,
herein	herein incorporated by	granulomatous disease,
refere	reference in its entirety. Mast	inflammatory bowel disease,
cells t	cells that may be used	sepsis, neutropenia,
accor	according to these assays are	neutrophilia, psoriasis,
public	publicly available (e.g.,	suppression of immune
throug	through the ATCC).	reactions to transplanted
Exem	Exemplary human mast cells	organs and tissues, hemophilia,

				that may be used according to these assays include the HMC- 1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
463	HPTVX32	1411	Hexosaminidase in RBL-2H3	immature mast cells.	
464	HPVAB94	1412	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and

response ele	response element activity of	inflammatory disorders. An
polypeptide	polypeptides of the invention	additional highly preferred
(including a	(including antibodies and	indication is infection (e.g., an
agonists or	agonists or antagonists of the	infectious disease as described
invention) i	invention) include assays	below under "Infectious
disclosed in	disclosed in Berger et al., Gene	Disease"). Preferred
66:1-10 (19	66:1-10 (1998); Cullen and	indications include neoplastic
Malm, Metl	Malm, Methods in Enzymol	diseases (e.g., leukemia,
 216:362-36	216:362-368 (1992); Henthorn	lymphoma, and/or as described
et al., Proc	et al., Proc Natl Acad Sci USA	below under
85:6342-63	85:6342-6346 (1988); Serfling	"Hyperproliferative
 et al., Bioch	et al., Biochim Biophys Acta	Disorders"). Preferred
1498(1):1-1	1498(1):1-18 (2000); De Boer	indications include neoplasms
et al., Int J l	et al., Int J Biochem Cell Biol	and cancers, such as, for
31(10):122	31(10):1221-1236 (1999);	example, leukemia, lymphoma,
Fraser et al.	Fraser et al., Eur J Immunol	and prostate, breast, lung,
29(3):838-8	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
Yeseen et a	Yeseen et al., J Biol Chem	stomach, brain, liver and
 268(19):142	268(19):14285-14293 (1993),	urinary cancer. Other preferred
the contents	the contents of each of which	indications include benign
are herein ii	are herein incorporated by	dysproliferative disorders and
reference in	reference in its entirety. T	pre-neoplastic conditions, such
cells that may be used	nay be used	as, for example, hyperplasia,
according to	according to these assays are	metaplasia, and/or dysplasia.
publicly ava	publicly available (e.g.,	Preferred indications also
through the ATCC).	ATCC).	include anemia, pancytopenia,
Exemplary	Exemplary human T cells that	leukopenia, thrombocytopenia,
 may be use	may be used according to these	Hodgkin's disease, acute
assays inclu	assays include the SUPT cell	lymphocytic anemia (ALL),
line, which	line, which is a suspension	plasmacytomas, multiple
culture of II	culture of IL-2 and IL-4	myeloma, Burkitt's lymphoma,

				responsive T cells.	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
	HPWAY46	1413	SEAP in 293/ISRE		asthma and allergy.
465	HPW A V46	1413	SEAD in HIB/CDE		
465	OF LAW III	1415			
	HPWAY46	1413	Activation of	This reporter assay measures	Highly preferred indications
465			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include

antagonists of the invention) to	autoimmune diseases (e.g.,
regulate GATA3 transcription	rheumatoid arthritis, systemic
factors and modulate	lupus erythematosis, multiple
expression of mast cell genes	sclerosis and/or as described
important for immune response	below) and
development. Exemplary	immunodeficiencies (e.g., as
assays for transcription	described below). Preferred
through the GATA3 response	indications include neoplastic
element that may be used or	diseases (e.g., leukemia,
routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
activity of polypeptides of the	pancreatic, esophageal,
invention (including antibodies	stomach, brain, liver, and
and agonists or antagonists of	urinary tract cancers and/or as
the invention) include assays	described below under
disclosed in Berger et al., Gene	"Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);	Preferred indications include
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
contents of each of which are	lymphoma, arthritis, AIDS,
herein incorporated by	granulomatous disease,

				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HPWAY46	1413	Activation of	This reporter assay measures	Highly preferred indications
465			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
		_	as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include

(including antibodies and	autoimmune diseases (e.g.,
agonists or antagonists of the	rheumatoid arthritis, systemic
invention) to regulate NFAT	lupus erythematosis, multiple
transcription factors and	sclerosis and/or as described
modulate expression of genes	below) and
 involved in	immunodeficiencies (e.g., as
   immunomodulatory functions.	described below). Preferred
Exemplary assays for	indications include neoplastic
transcription through the	diseases (e.g., leukemia,
NFAT response element that	lymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
(including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et al., J Immunol	leukemias, Hodgkin's disease,
165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
 16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
al., J Exp Med 188:527-537	granulomatous disease,

				which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
HPW	HPWAY46	1413	IL-6 in HUVEC		
HPW	HPWAY46	1413	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells.	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An

transcription through the CD28		alternative highly preferred
response element that may be		embodiment of the invention
used or routinely modified to	ed to	includes a method for
test CD28-response element	nent	inhibiting the activation of
activity of polypeptides of the	of the	and/or inactivating T cells.
 invention (including antibodies	ibodies	A highly preferred
and agonists or antagonists of	ists of	embodiment of the invention
the invention) include assays	ssays	includes a method for
disclosed in Berger et al., Gene	l., Gene	stimulating (e.g., increasing)
66:1-10 (1998); Cullen and	and	IL-2 production. An alternative
Malm, Methods in Enzymol	/mol	highly preferred embodiment
216:362-368 (1992); Henthorn	enthorn	of the invention includes a
 et al., Proc Natl Acad Sci USA	ci USA	method for inhibiting (e.g.,
85:6342-6346 (1988);		reducing) IL-2 production.
McGuire and Iacobelli, J	ſ	Additional highly preferred
Immunol 159(3):1319-1327	327	indications include
(1997); Parra et al., J Immunol	lounuu	inflammation and
166(4):2437-2443 (2001); and	l); and	inflammatory disorders.
Butscher et al., J Biol Chem	hem	Highly preferred indications
 3(1):552-560 (1998), the	<b>.</b>	include autoimmune diseases
 contents of each of which are	ch are	(e.g., rheumatoid arthritis,
herein incorporated by		systemic lupus erythematosis,
 reference in its entirety.	L	multiple sclerosis and/or as
cells that may be used		described below),
 according to these assays are	's are	immunodeficiencies (e.g., as
publicly available (e.g.,		described below), boosting a T
through the ATCC).		cell-mediated immune
Exemplary human T cells that	lls that	response, and suppressing a T
may be used according to these	to these	cell-mediated immune
 assays include the JURKAT	KAT	response. An additional highly
cell line, which is a suspension	$\neg$	preferred indication includes

produce IL-2 when stimulated.	culture of	culture of leukemia cells that	infection (e.g., AIDS, and/or as
	[] produce []		described below under
	-		"Infectious Disease").
			Highly preferred indications
			include neoplastic diseases
			(e.g., melanoma, renal cell
		-	carcinoma, leukemia,
			lymphoma, and/or as described
			below under
			"Hyperproliferative
			Disorders"). Highly preferred
			indications include neoplasms
			and cancers, such as, for
			example, melanoma (e.g.,
			metastatic melanoma), renal
			cell carcinoma (e.g., metastatic
			renal cell carcinoma),
			leukemia, lymphoma (e.g., T
	-		cell lymphoma), and prostate,
			breast, lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
	-		conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			A highly preferred indication
			is infection (e.g., tuberculosis,
			infections associated with

 granulomatous disease, and	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). A highly preferred	indication is AIDS.	Additional highly preferred	indications include suppression	of immune reactions to	transplanted organs and/or	tissues, uveitis, psoriasis, and	tropical spastic paraparesis.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,
																								-			_			

					meningitis, Lyme Disease,
					asthma and allergy.
	HPWAY46	1413	SEAP in Jurkat/IL4		
465			promoter		
	HPWAY46	1413	SEAP in Jurkat/IL4		
465			promoter (antiCD3 co-stim)		
	HPWAY46	1413	Activation of	Assays for the activation of	Highly preferred indications
465			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
				invention (including antibodies	example, leukemia, lymphoma
				and agonists or antagonists of	(e.g., T cell lymphoma,
				the invention) to regulate	Burkitt's lymphoma, non-
				STAT transcription factors and	Hodgkins lymphoma,
				modulate gene expression	Hodgkin"s disease),
				involved in a wide variety of	melanoma, and prostate,
				cell functions. Exemplary	breast, lung, colon, pancreatic,
				assays for transcription	esophageal, stomach, brain,
				through the GAS response	liver and urinary cancer. Other
				element that may be used or	preferred indications include
				routinely modified to test	benign dysproliferative
				GAS-response element activity	disorders and pre-neoplastic
				of polypeptides of the	conditions, such as, for
				invention (including antibodies	example, hyperplasia,
				and agonists or antagonists of	metaplasia, and/or dysplasia.
				the invention) include assays	Preferred indications include

disclosed in Berger et al Gene	autoimmune diseases (e.g.,
	rheumatoid arthritis, systemic
Malm, Methods in Enzymol	lupus erythematosis, multiple
216:362-368 (1992); Henthorn	sclerosis and/or as described
et al., Proc Natl Acad Sci USA	below), immunodeficiencies
85:6342-6346 (1988);	(e.g., as described below),
Matikainen et al., Blood	boosting a T cell-mediated
93(6):1980-1991 (1999); and	immune response, and
Henttinen et al., J Immunol	suppressing a T cell-mediated
155(10):4582-4587 (1995), the	immune response. Additional
contents of each of which are	preferred indications include
herein incorporated by	inflammation and
reference in its entirety.	inflammatory disorders.
Exemplary human T cells,	Highly preferred indications
such as the SUPT cell line, that	include blood disorders (e.g.,
may be used according to these	as described below under
assays are publicly available	"Immune Activity", "Blood-
(e.g., through the ATCC).	Related Disorders", and/or
	"Cardiovascular Disorders"),
	and infection (e.g., viral
	infections, tuberculosis,
	infections associated with
	chronic granulomatosus
	disease and malignant
	osteoporosis, and/or an
	infectious disease as described
	below under "Infectious
	Disease"). An additional
	preferred indication is
	idiopathic pulmonary fibrosis.
	Preferred indications include

anemia, pancytopenia, leukopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	ctivation of A highly preferred indication is allergy. Sers and Another highly preferred indication is asthma.  Referred indication is asthma.  Additional highly preferred indications include inflammation and inflammation and inflammation and inflammatory disorders.  The invention Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or pression of Preferred indications include Exemplary Preferred indications include
	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary
	Activation of transcription through STAT6 response element in immune cells (such as T-cells).
	1413
	HPWAY46
	465

assavs for transcription		autoimmune diseases (e.g.,
through the STAT6 response	onse	rheumatoid arthritis, systemic
element that may be used or	e used or	lupus erythematosis, multiple
routinely modified to test	to test	sclerosis and/or as described
STAT6 response element	lement	below) and
activity of the polypeptides of	peptides of	immunodeficiencies (e.g., as
the invention (including	uding	described below).
antibodies and agonists or	nists or	Preferred indications include
antagonists of the invention)		neoplastic diseases (e.g.,
include assays disclosed in		leukemia, lymphoma,
Berger et al., Gene 66:1-10		melanoma, and/or as described
(1998); Cullen and Malm,	Malm,	below under
Methods in Enzymol 216:362-		"Hyperproliferative
368 (1992); Henthorn et al.,	orn et al.,	Disorders"). Preferred
Proc Natl Acad Sci USA	i USA	indications include neoplasms
85:6342-6346 (1988); Georas	38); Georas	and cancers, such as, leukemia,
et al., Blood 92(12):4529-4538	):4529-4538	lymphoma, melanoma, and
(1998); Moffatt et al.,	al.,	prostate, breast, lung, colon,
Transplantation 69(7):1521-	(7):1521-	pancreatic, esophageal,
1523 (2000); Curiel et al., Eur	el et al., Eur	stomach, brain, liver and
J Immunol 27(8):1982-1987	982-1987	urinary cancer. Other preferred
(1997); and Masuda et al., J		indications include benign
Biol Chem 275(38):29331-	):29331-	dysproliferative disorders and
29337 (2000), the contents of	contents of	pre-neoplastic conditions, such
each of which are herein	herein	as, for example, hyperplasia,
incorporated by reference in its	its	metaplasia, and/or dysplasia.
entirety. T cells that may be	lat may be	Preferred indications include
used according to these assays	these assays	anemia, pancytopenia,
are publicly available (e.g.,	ble (e.g.,	leukopenia, thrombocytopenia,
through the ATCC).		Hodgkin's disease, acute
Exemplary T cells that may be		lymphocytic anemia (ALL),

			used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious
HPWDJ42	1414	Inhibition of squalene synthetase gene transcription.	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a	

				human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein	
				incorporated by reference in its entirety.	
	HPWDJ42	1414	Activation of	Assays for the activation of	Highly preferred indications
466			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
			cells (such as T-	are well-known in the art and	Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described

	invention) include assays	below under "Infectious
	disclosed in Berner et al Gene	Disease") Preferred
	46.1 10 (1009): Cullon and	indications include acculaction
	00:1-10 (1996), Cullell alid	maicanons menude neopiasuc
 	Malm, Methods in Enzymol	diseases (e.g., leukemia,
 	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	 et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988); Serfling	"Hyperproliferative
	et al., Biochim Biophys Acta	Disorders"). Preferred
 	1498(1):1-18 (2000); De Boer	indications include neoplasms
	et al., Int J Biochem Cell Biol	and cancers, such as, for
 	31(10):1221-1236 (1999);	example, leukemia, lymphoma,
 	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	 268(19):14285-14293 (1993),	urinary cancer. Other preferred
 	the contents of each of which	indications include benign
	 are herein incorporated by	dysproliferative disorders and
 	 reference in its entirety. T	pre-neoplastic conditions, such
 	cells that may be used	as, for example, hyperplasia,
	 according to these assays are	metaplasia, and/or dysplasia.
	publicly available (e.g.,	Preferred indications also
	 through the ATCC).	include anemia, pancytopenia,
 	Exemplary human T cells that	leukopenia, thrombocytopenia,
 	may be used according to these	Hodgkin's disease, acute
	assays include the JURKAT	lymphocytic anemia (ALL),
 	 cell line, which is a suspension	plasmacytomas, multiple
	 culture of leukemia cells that	myeloma, Burkitt's lymphoma,
	produce IL-2 when stimulated.	arthritis, AIDS, granulomatous
 		disease, inflammatory bowel
		disease, sepsis, neutropenia,
		neutrophilia, psoriasis,

. v,		<u></u>			
suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative	Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders",	and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under	"Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders.
	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or	apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of	the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell	(e.g. T-cell) proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to	test JNK and p38 kinase- induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol
	Activation of T-Cell p38 or JNK Signaling Pathway.				
	1415				
	HPZAB47				
	467				

Chem 379(8-9):1101-1110	Highly preferred indications
(1998); Gupta et al., Exp Cell	also include neoplastic
Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
Kyriakis JM, Biochem Soc	lymphoma, and/or as described
Symp 64:29-48 (1999); Chang	below under
and Karin, Nature	"Hyperproliferative
410(6824):37-40 (2001); and	Disorders"). Highly preferred
Cobb MH, Prog Biophys Mol	indications include neoplasms
Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
the contents of each of which	lymphoma, prostate, breast,
 are herein incorporated by	lung, colon, pancreatic,
reference in its entirety. T	esophageal, stomach, brain,
cells that may be used	liver, and urinary cancer. Other
according to these assays are	preferred indications include
publicly available (e.g.,	benign dysproliferative
through the ATCC).	disorders and pre-neoplastic
Exemplary mouse T cells that	conditions, such as, for
may be used according to these	
assays include the CTLL cell	metaplasia, and/or dysplasia.
 line, which is an IL-2	Preferred indications include
dependent suspension-culture	arthritis, asthma, AIDS,
cell line with cytotoxic	allergy, anemia, pancytopenia,
activity.	leukopenia, thrombocytopenia,
	Hodgkin"s disease, acute
	lymphocytic anemia (ALL),
	plasmacytomas, multiple
	myeloma, Burkitt"s lymphoma,
	granulomatous disease,
	inflammatory bowel disease,
	sepsis, psoriasis, suppression
	of immune reactions to

				transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
HPZAB47	1415	CD152 in Human T cells		
HPZAB47	1415	Activation of	Assays for the activation of	Preferred embodiments of the
		transcription	transcription through the	invention include using
		through NFKB	NFKB response element are	polypeptides of the invention
		response element in	well-known in the art and may	(or antibodies, agonists, or
		neuronal cells (such	be used or routinely modified	antagonists thereof) in
		as SKNMC cells).	to assess the ability of	detection, diagnosis,
			polypeptides of the invention	prevention, and/or treatment of
			(including antibodies and	Neurological Diseases and
			agonists or antagonists of the	Disorders (e.g. Alzheimer"s
			invention) to regulate NFKB	Disease, Parkinson"s Disease,
			transcription factors and	Brain Cancer, Seizures).
			modulate expression of	
			neuronal genes. Exemplary	
			assays for transcription	
			through the NFKB response	
			element that may be used or	
			routinely modified to test	
			NFKB-response element	
			activity of polypeptides of the	
			invention (including antibodies	
			and agonists or antagonists of	
			the invention) include assays	
			disclosed in: Gill JS, et al.,	
			Neurobiol Dis, 7(4):448-461	
			(2000); Tamatani M, et al., J	
			Biol Chem, 274(13):8531-	

en 46 46 al, 0 1 re are says hat hese	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity",
8538 (1999); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary neuronal cells that may be used according to these assays include the SKNMC neuronal cell line.	
	Activation of T-Cell p38 or JNK Signaling Pathway.
	HRAAB15
	468

	the invention (including	and/or "Blood-Related
	antibodies and agonists or	Disorders"), and infection
	antagonists of the invention) to	(e.g., an infectious disease as
	promote or inhibit immune cell	described below under
	(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
	activation, and apoptosis.	preferred indications include
	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other
	according to these assays are	preferred indications include
!	publicly available (e.g.,	benign dysproliferative

				through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
				assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt"s lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HRAAB15	1416	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
468			IFNgamma using a	a central role in the immune	embodiment of the invention
			T cells	system and is considered to be	includes a method for
				a proinflammatory cytokine.	stimulating the production of
				IFNg promotes TH1 and	IFNg. An alternative highly
				inhibits TH2 differentiation;	preferred embodiment of the
				promotes IgG2a and inhibits	invention includes a method
				IgE secretion; induces	bitin
				macrophage activation; and	IFNg. Highly preferred
				increases MHC expression.	ons
				Assays for immunomodulatory	disorders (e.g., as described
				proteins produced by T cells	below under "Immune

and NK cells that regulate a	Activity", "Blood-Related
variety of inflammatory	Disorders", and/or
activities and inhibit TH2	"Cardiovascular Disorders"),
helper cell functions are well	and infection (e.g., viral
known in the art and may be	infections, tuberculosis,
used or routinely modified to	infections associated with
assess the ability of	chronic granulomatosus
polypeptides of the invention	disease and malignant
(including antibodies and	osteoporosis, and/or as
agonists or antagonists of the	described below under
invention) to mediate	"Infectious Disease"). Highly
immunomodulation, regulate	preferred indications include
inflammatory activities,	autoimmune disease (e.g.,
modulate TH2 helper cell	rheumatoid arthritis, systemic
function, and/or mediate	lupus erythematosis, multiple
humoral or cell-mediated	sclerosis and/or as described
immunity. Exemplary assays	below), immunodeficiency
that test for	(e.g., as described below),
immunomodulatory proteins	boosting a T cell-mediated
evaluate the production of	immune response, and
cytokines, such as Interferon	suppressing a T cell-mediated
gamma (IFNg), and the	immune response. Additional
activation of T cells. Such	highly preferred indications
assays that may be used or	include inflammation and
routinely modified to test	inflammatory disorders.
immunomodulatory activity of	Additional preferred
polypeptides of the invention	indications include idiopathic
(including antibodies and	pulmonary fibrosis. Highly
agonists or antagonists of the	preferred indications include
invention) include the assays	neoplastic diseases (e.g.,
disclosed in Miraglia et al., J	leukemia, lymphoma,

	Biomolecular Screening 4:193-	193-   melanoma, and/or as described
	204 (1999): Rowland et al	
	"I ymphocytes: a practical	
	approach" Chapter 6:138-160	
	(2000); Gonzalez et al., J Clin	· <u>-</u>
	Lab Anal 8(5):225-233 (1995);	
	Billiau et al., Ann NY Acad	d example, leukemia, lymphoma,
	Sci 856:22-32 (1998); Boehm	hm   melanoma, and prostate,
	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
	15:749-795 (1997), and	esophageal, stomach, brain,
	Rheumatology (Oxford)	liver and urinary cancer. Other
-	38(3):214-20 (1999), the	preferred indications include
	contents of each of which are	re benign dysproliferative
	herein incorporated by	disorders and pre-neoplastic
	reference in its entirety.	conditions, such as, for
	Human T cells that may be	example, hyperplasia,
	used according to these assays	ays   metaplasia, and/or dysplasia.
	may be isolated using	Preferred indications include
	techniques disclosed herein or	or anemia, pancytopenia,
	otherwise known in the art.	leukopenia, thrombocytopenia,
	Human T cells are primary	Hodgkin's disease, acute
	human lymphocytes that	lymphocytic anemia (ALL),
	mature in the thymus and	plasmacytomas, multiple
	express a T Cell receptor and	nd   myeloma, Burkitt's lymphoma,
	CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
	cells mediate humoral or cell-	ell- disease, inflammatory bowel
	mediated immunity and may	y disease, sepsis, neutropenia,
	be preactivated to enhance	neutrophilia, psoriasis,
	responsiveness to	suppression of immune
	immunomodulatory factors.	. reactions to transplanted
		organs and tissues,

					hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
					asthma and allergy.
	HRABA80	1417	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
469				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred
				routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
				cells) by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other

disclosed in: Shimizu, H., et	diseases and disorders as
al., Endocr J, 47(3):261-9	described in the
(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
17 (1999); Filipsson, K., et al.,	endocrine disorders (as
Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
(1998); Olson, L.K., et al., J	Disorders" section below),
Biol Chem, 271(28):16544-52	neuropathy, vision impairment
(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
Journal of Biomolecular	blindness), ulcers and impaired
Screening, 4:193-204 (1999),	wound healing, and infection
the contents of each of which	(e.g., infectious diseases and
is herein incorporated by	disorders as described in the
reference in its entirety.	"Infectious Diseases" section
Pancreatic cells that may be	below, especially of the
used according to these assays	urinary tract and skin), carpal
are publicly available (e.g.,	tunnel syndrome and
through the ATCC) and/or	Dupuytren's contracture).
may be routinely generated.	An additional highly preferred
Exemplary pancreatic cells that	indication is obesity and/or
may be used according to these	complications associated with
assays include HITT15 Cells.	obesity. Additional highly
HITT15 are an adherent	preferred indications include
epithelial cell line established	weight loss or alternatively,
from Syrian hamster islet cells	weight gain. Additional highly
transformed with SV40. These	preferred indications are
cells express glucagon,	complications associated with
somatostatin, and	insulin resistance.
glucocorticoid receptors. The	
cells secrete insulin, which is	
stimulated by glucose and	

				glucagon and suppressed by somatostatin or	
				glucocorticoids. ATTC# CRL-	
				1777 Refs: Lord and	
				Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
	HRABA80	1417	CD152 in Human T		
469			cells		
	HRABA80	1417	Activation of	Kinase assay. Kinase assays,	A highly preferred
469			Endothelial Cell	for example an Elk-1 kinase	embodiment of the invention
			ERK Signaling	assay, for ERK signal	includes a method for
			Pathway.	transduction that regulate cell	stimulating endothelial cell
				proliferation or differentiation	growth. An alternative highly
				are well known in the art and	preferred embodiment of the
				may be used or routinely	invention includes a method
				modified to assess the ability	for inhibiting endothelial cell
				of polypeptides of the	growth. A highly preferred
				invention (including antibodies	embodiment of the invention
				and agonists or antagonists of	includes a method for
				the invention) to promote or	stimulating endothelial cell
				inhibit cell proliferation,	proliferation. An alternative
				activation, and differentiation.	highly preferred embodiment
				Exemplary assays for ERK	of the invention includes a
				kinase activity that may be	method for inhibiting
				used or routinely modified to	endothelial cell proliferation.
				test ERK kinase-induced	A highly preferred
				activity of polypeptides of the	embodiment of the invention
				invention (including antibodies	includes a method for
				and agonists or antagonists of	stimulating apoptosis of

the	the invention) include the	endothelial cells. An
ass	assays disclosed in Forrer et	alternative highly preferred
al.,	al., Biol Chem 379(8-9):1101-	embodiment of the invention
 111	1110 (1998); Berra et al.,	includes a method for
Bic	Biochem Pharmacol	inhibiting (e.g., decreasing)
)09	60(8):1171-1178 (2000);	apoptosis of endothelial cells.
Gu	Gupta et al., Exp Cell Res	A highly preferred
247	247(2):495-504 (1999); Chang	embodiment of the invention
and	and Karin, Nature	includes a method for
410	410(6824):37-40 (2001); and	stimulating (e.g., increasing)
Col	Cobb MH, Prog Biophys Mol	endothelial cell activation. An
Bic	Biol 71(3-4):479-500 (1999);	alternative highly preferred
the	the contents of each of which	embodiment of the invention
are	are herein incorporated by	includes a method for
refe	reference in its entirety.	inhibiting the activation of
Enc	Endothelial cells that may be	(e.g., decreasing) and/or
nse	used according to these assays	inactivating endothelial cells.
are	are publicly available (e.g.,	A highly preferred
thre	through the ATCC).	embodiment of the invention
Exe	Exemplary endothelial cells	includes a method for
tha	that may be used according to	stimulating endothelial cell
the	these assays include human	differentiation. An alternative
mn	umbilical vein endothelial cells	highly preferred embodiment
IH)	(HUVEC), which are	of the invention includes a
end	endothelial cells which line	method for inhibiting
ven	venous blood vessels, and are	endothelial cell differentiation.
vai	involved in functions that	A highly preferred
inc	include, but are not limited to,	embodiment of the invention
 ang	angiogenesis, vascular	includes a method for
per	permeability, vascular tone,	stimulating angiogenisis. An
and	and immune cell extravasation.	alternative highly preferred

		Highly preferred indications
		ingling prototogramons
_		include cardiovascular,
		endothelial and/or angiogenic
		disorders (e.g., systemic
		disorders that affect vessels
		such as diabetes mellitus, as
		well as diseases of the vessels
		themselves, such as of the
		arteries, capillaries, veins
		and/or lymphatics). Highly
		preferred are indications that
		stimulate angiogenesis and/or
		cardiovascularization. Highly
		preferred are indications that
		inhibit angiogenesis and/or
		cardiovascularization.
		Highly preferred indications
		include antiangiogenic activity
		to treat solid tumors,
		leukemias, and Kaposi"s
		sarcoma, and retinal disorders.
		Highly preferred indications
		include neoplasms and cancer,
		such as, Kaposi"s sarcoma,
		hemangioma (capillary and
		cavernous), glomus tumors,
		telangiectasia, bacillary
		angiomatosis,
		hemangioendothelioma,
		angiosarcoma,
		haemangiopericytoma,

		lymphangioma
		1bar all and a little bit.
		lymphanglosarcoma. Highly
		preferred indications also
		include cancers such as,
		prostate, breast, lung, colon,
		pancreatic, esophageal,
		stomach, brain, liver, and
		urinary cancer. Preferred
		indications include benign
		dysproliferative disorders and
-		pre-neoplastic conditions, such
		as, for example, hyperplasia,
		metaplasia, and/or dysplasia.
		Highly preferred indications
	***************************************	also include arterial disease,
		such as, atherosclerosis,
		hypertension, coronary artery
	-	disease, inflammatory
		vasculitides, Reynaud"s
		disease and Reynaud"s
		phenomenom, aneurysms,
		restenosis; venous and
		lymphatic disorders such as
		thrombophlebitis,
		lymphangitis, and
		lymphedema; and other
		vascular disorders such as
		peripheral vascular disease,
		and cancer. Highly
		preferred indications also
		include trauma such as

tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lestons), implant fixation, scarring, ischemia repertusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal findiue, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coaqulative disorders, vascularitis. Jumph angiogenesis; sexual disorders age-related macular degeneration, and treatment forevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include blood disorders (e.g. as described below under "Immune Activity", "Blood-"Immune Activity", "Blood-"" "Immune Activity", "Blood-"" "Immune Activity", "Blood-"			wounds hums and injured
such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia repertusion injury. Theumatoid arthritis, cerebrovascular diseases such as acute renal diseases such as acute renal fialture, and osteoporosis.  Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment prevention of rendometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, and vascular valve disease, and vascular disease, and described below under "Immune Activity", "Blood-	_		figure (o & woomles in in
such as, nijury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia repetrision injury, rheumatoid arthritis, cerebrovascular disease, renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotid and coagulative disorders, vascularitis, Jymph angiogenesis, sexual disorders age-related macular degeneration, and treatment Prevention of endometricosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			ussue (e.g., vascular mjury
abloon angioplasty, and abloon angioplasty, and aplant fixation; estorins, implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal fitalture, and ostoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macutar degeneration, and treatment /prevention of endomentriosis and related conditions. Additional highly preferred indications include fibromas, heart valve disease, and vascular disease, and vascular disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			such as, injury resulting from
implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, scerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis.  Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment of prevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, and vascular disease, and described below under diseave, as a described below under disman-devivity, "Blood-"Immune Activity", "Blood-"Immune Activity", "Blood-"			balloon angioplasty, and
implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis.  Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment /prevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, and vascular disease, and vascular disease, and vascular disease, and esercibed below under disearched blood disorders (e.g., as described below under dismany). "Blood-"filmmune Activity", "Blood-"filmmune Activity", "Blood-"filmmune Activity", "Blood-"filmmune Activity", "Blood-"			atheroschlerotic lesions),
ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment (prevention of endometriosis and related conditions Additional highly preferred indications include fibromas, heart disease, and vascular disease, and vascular disease, Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			implant fixation, scarring,
rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment (prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease, Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			ischemia reperfusion injury,
diseases such as acute renal failure, and osteoporosis.  Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, thrombotic and coagulative disorders, age-related macular degeneration, and treatment of prevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include fibromas, photod disorders (e.g., as described below under "Immune Activity", "Blood-"Immune Activity", "Blood-"Immune Activity", "Blood-"		-	rheumatoid arthritis,
diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment / prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart disease, and vascular disease, Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			cerebrovascular disease, renal
failure, and osteoporosis.  Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment hyperention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart valve disease, and vascular disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-"Immune Activity", "Blood-"Immune Activity", "Blood-"Immune Activity", "Blood-"			diseases such as acute renal
Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment prevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-"Immune Activity", "Blood-"	 -	- 14	failure, and osteoporosis.
indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, Iymph angiogenesis, sexual disorders age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			Additional highly preferred
graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment //prevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-"Immune Activity", "Blood-"			indications include stroke,
other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment // prevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-"Immune Activity", "Blood-"			graft rejection, diabetic or
and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment /prevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-"Immune Activity", "Blood-"			other retinopathies, thrombotic
vascularitis, lymph angiogenesis, sexual disorders age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			and coagulative disorders,
angiogenesis, sexual disorders age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease, and vascular disease, and blood disorders (e.g., as described below under "Immune Activity", "Blood-			vascularitis, lymph
age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			angiogenesis, sexual disorders,
degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			age-related macular
/prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			degeneration, and treatment
and related conditions.  Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			/prevention of endometriosis
Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			and related conditions.
indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			Additional highly preferred
heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			indications include fibromas,
heart valve disease, and vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			heart disease, cardiac arrest,
vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-			heart valve disease, and
Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-	 		vascular disease.
blood disorders (e.g., as described below under "Immune Activity", "Blood-			Preferred indications include
described below under "Immune Activity", "Blood-			blood disorders (e.g., as
"Immune Activity", "Blood-			described below under
			"Immune Activity", "Blood-

					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HRACD15	1418	Regulation of	Assays for the regulation of	A highly preferred
470			transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
		_	hepatocytes	may be used or routinely	indication is a complication
				modified to assess the ability	associated with diabetes (e.g.,
				of polypeptides of the	diabetic retinopathy, diabetic
				invention (including antibodies	nephropathy, kidney disease
	-			and agonists or antagonists of	(e.g., renal failure,
				the invention) to regulate	nephropathy and/or other
				transcription of Malic Enzyme,	diseases and disorders as
				a key enzyme in lipogenesis.	described in the "Renal
				Malic enzyme is involved in	Disorders" section below),
				lipogenesisand its expression is	diabetic neuropathy, nerve

nts as as as as as and may other do to do to tion tion tion the the the to the to the tall, and tall, tall,		
stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors. Exemplary assays that may be used or routinely modified to test for regulation of Malic Enzyme (in hepatocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Streeper, R.S., et al., Mol Endocrinol, 12(11):1778-91 (1998); Garcia-Jimenez, C., et al., Mol Endocrinol, 8(10):1361-9 (1994); Barroso, I., et al., J Biol Chem, 274(25):17997-8004 (1999); Ijpenberg, A., et al., J Biol Chem, 272(32):20108-20117 (1997); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol.	stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors. Exemplary assays that may be used or routinely modified to test for regulation of transcription of Malic Enzyme (in hepatocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Streeper, R.S., et al., Mol Endocrinol, 12(11):1778-91 (1998); Garcia-Jimenez, C., et al., Mol Endocrinol, 8(10):1361-9 (1994); Barroso, I., et al., J Biol Chem, 274(25):17997- 8004 (1999); Ijpenberg, A., et al., J Biol Chem, 272(32):20108-20117 (1997); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol.	stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors. Exemplary assays that may be used or routinely modified to test for regulation of transcription of Malic Enzyme (in hepatocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Streeper, R.S., et al., Mol Endocrinol, 12(11):1778-91 (1998); Garcia-Jimenez, C., et al., Mol Endocrinol, 8(10):1361-9 (1994); Barroso, I., et al., J Biol Chem, 274(25):17997- 8004 (1999); lipenberg, A., et al., J Biol Chem, 272(32):20108-20117 (1997); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al.,

				herein incorporated by	Dupuytren's contracture).
				reference in its entirety.	indication is obesity and/or
				Hepatocytes that may be used	complications associated with
	_			according to these assays are	obesity. Additional highly
				publicly available (e.g.,	preferred indications include
				through the ATCC) and/or	or alterna
	_			may be routinely generated.	weight gain. Aditional
				Exemplary hepatocytes that	highly preferred indications are
				may be used according to these	complications associated with
				assays includes the mouse	insulin resistance.
	-			3T3-L1 cell line. 3T3-L1 is a	
				mouse preadipocyte cell line	
	-			(adherent). It is a continuous	
				substrain of 3T3 fibroblasts	
				developed through clonal	
<del>.,</del>				isolation. Cells undergo a pre-	
				adipocyte to adipose-like	
				conversion under appropriate	
				differentiation culture	
				conditions.	
HRA	HRACD15	1418	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
!				antibodies and agonists or	Disorders"), and infection

antagonists of the invention) to	(e.g., an infectious disease as
promote or inhibit immune cell	described below under
(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
activation, and apoptosis.	preferred indications include
Exemplary assays for JNK and	autoimmune diseases (e.g.,
p38 kinase activity that may be	rheumatoid arthritis, systemic
used or routinely modified to	lupus erythematosis, multiple
test JNK and p38 kinase-	sclerosis and/or as described
induced activity of	below) and
polypeptides of the invention	immunodeficiencies (e.g., as
(including antibodies and	described below). Additional
agonists or antagonists of the	highly preferred indications
invention) include the assays	include inflammation and
disclosed in Forrer et al., Biol	inflammatory disorders.
Chem 379(8-9):1101-1110	Highly preferred indications
(1998); Gupta et al., Exp Cell	also include neoplastic
Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
Kyriakis JM, Biochem Soc	lymphoma, and/or as described
Symp 64:29-48 (1999); Chang	below under
and Karin, Nature	"Hyperproliferative
410(6824):37-40 (2001); and	Disorders"). Highly preferred
Cobb MH, Prog Biophys Mol	indications include neoplasms
Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
the contents of each of which	lymphoma, prostate, breast,
are herein incorporated by	lung, colon, pancreatic,
reference in its entirety. T	esophageal, stomach, brain,
cells that may be used	liver, and urinary cancer. Other
according to these assays are	preferred indications include
publicly available (e.g.,	benign dysproliferative
through the ATCC).	disorders and pre-neoplastic
Exemplary mouse T cells that	conditions, such as, for

				may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
470	HRACD15	1418	SEAP in HIB/CRE		
470	HRACD15	1418	Regulation of apoptosis of immune cells (such as mast cells).	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.

cells are found in connective	and mucosal tissues throughout	the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are
		<b>1</b>		3		1	2				I				-			1							7					
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HRACD15	1418 SEAP in Jurkat/IL4 promoter (antiCD3	_	reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	
	Production of IL-6		IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Belated Disorders", and/or

expression level is strongly	"Cardiovascular Disorders"),
regulated by cytokines, growth	and infection (e.g., as
factors, and hormones are well	described below under
known in the art and may be	"Infectious Disease"). Highly
used or routinely modified to	preferred indications include
assess the ability of	autoimmune diseases (e.g.,
polypeptides of the invention	rheumatoid arthritis, systemic
(including antibodies and	lupus erythematosis, multiple
agonists or antagonists of the	sclerosis and/or as described
invention) to mediate	below) and
immunomodulation and	immunodeficiencies (e.g., as
differentiation and modulate T	described below). Highly
cell proliferation and function.	preferred indications also
Exemplary assays that test for	include boosting a B cell-
immunomodulatory proteins	mediated immune response
evaluate the production of	and alternatively suppressing a
cytokines, such as IL-6, and	B cell-mediated immune
the stimulation and	response. Highly preferred
upregulation of T cell	indications include
proliferation and functional	inflammation and
activities. Such assays that	inflammatory
may be used or routinely	disorders.Additional highly
modified to test	preferred indications include
immunomodulatory and	asthma and allergy. Highly
diffferentiation activity of	preferred indications include
polypeptides of the invention	neoplastic diseases (e.g.,
(including antibodies and	myeloma, plasmacytoma,
agonists or antagonists of the	leukemia, lymphoma,
invention) include assays	melanoma, and/or as described
disclosed in Miraglia et al., J	below under
Biomolecular Screening 4:193-	"Hyperproliferative

204(1	204(1999); Rowland et al.,	Disorders"). Highly preferred
"Lym	"Lymphocytes: a practical	indications include neoplasms
appro	160	and cancers, such as, myeloma,
(2000	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
Immr	Immunol 158:2919-2925	lymphoma, melanoma, and
(1997	(1997), the contents of each of	prostate, breast, lung, colon,
which	which are herein incorporated	pancreatic, esophageal,
by ref	by reference in its entirety.	stomach, brain, liver and
Hume	Human dendritic cells that may	urinary cancer. Other preferred
pe nae	be used according to these	indications include benign
assay	1g	dysproliferative disorders and
techn	techniques disclosed herein or	pre-neoplastic conditions, such
other	otherwise known in the art.	as, for example, hyperplasia,
Hume	Human dendritic cells are	metaplasia, and/or dysplasia.
antige	antigen presenting cells in	Preferred indications include
sasbe	suspension culture, which,	anemia, pancytopenia,
when	when activated by antigen	leukopenia, thrombocytopenia,
and/o	and/or cytokines, initiate and	Hodgkin's disease, acute
npreg	upregulate T cell proliferation	lymphocytic anemia (ALL),
and fu	and functional activities.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, and Lyme Disease.

					An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
472	HRDDV47	1420	CD71 in Human T cells		
472	HRDDV47	1420	IL-10 in Human T- cell 2B9		
473	HRDFD27	1421	Activation of transcription	Assays for the activation of transcription through the	A preferred embodiment of the invention includes a
)			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
		_		antibodies and agonists or	increasing) TNF alpha
-				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
	-			antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described

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					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
			-		Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
473	HRDFD27	1421	IL-10 in Human T-cell 2B9		
473	HRDFD27	1421	Activation of	Kinase assay. JNK and p38	A highly preferred
4/3			Endotnellal Cell	Kinase assays for signal	embodiniem of the myennon

p38 or JNK	transduction that regulate cell	includes a method for
Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
)	apoptosis are well known in	growth. An alternative highly
	the art and may be used or	preferred embodiment of the
	routinely modified to assess	invention includes a method
	the ability of polypeptides of	for inhibiting endothelial cell
	the invention (including	growth. A highly preferred
	antibodies and agonists or	embodiment of the invention
	antagonists of the invention) to	includes a method for
	promote or inhibit cell	stimulating endothelial cell
	proliferation, activation, and	proliferation. An alternative
	apoptosis. Exemplary assays	highly preferred embodiment
	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
-	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
	assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
 	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred

are	are herein incorporated by	embodiment of the invention
refer	reference in its entirety.	includes a method for
Ende	Endothelial cells that may be	inhibiting (e.g., decreasing) the
pesn	used according to these assays	activation of and/or
are	are publicly available (e.g.,	inactivating endothelial cells.
thro	through the ATCC).	A highly preferred
Exer	Exemplary endothelial cells	embodiment of the invention
that	that may be used according to	includes a method for
these	these assays include human	stimulating angiogenisis. An
quin	umbilical vein endothelial cells	alternative highly preferred
OH)	(HUVEC), which are	embodiment of the invention
endc	endothelial cells which line	includes a method for
nenc   neuc	venous blood vessels, and are	inhibiting angiogenesis. A
ovni	involved in functions that	highly preferred embodiment
inch	include, but are not limited to,	of the invention includes a
angi	angiogenesis, vascular	method for reducing cardiac
perm	permeability, vascular tone,	hypertrophy. An alternative
and	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as
		described below under
		"Hyperproliferative
		Disorders"), and disorders of
		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
		cardiomyopathy, valvular

	regurgi	regurgitation. left ventricular
	unjskp	dysfunction, atherosclerosis
	and ath	and atherosclerotic vascular
	disease	disease, diabetic nephropathy,
	intraca	intracardiac shunt, cardiac
	hypertr	hypertrophy, myocardial
	infarcti	infarction, chronic
	hemod	hemodynamic overload, and/or
	as desc	as described below under
	"Cardi	"Cardiovascular Disorders").
	Highly	Highly preferred indications
	include	include cardiovascular,
	endoth	endothelial and/or angiogenic
	disorde	disorders (e.g., systemic
	disorde	disorders that affect vessels
	such as	such as diabetes mellitus, as
	well as	well as diseases of the vessels
	themse	themselves, such as of the
	arteries	arteries, capillaries, veins
	and/or	and/or lymphatics). Highly
	preferr	preferred are indications that
	stimula	stimulate angiogenesis and/or
	cardiov	cardiovascularization. Highly
	preferr	preferred are indications that
-	inhibit	inhibit angiogenesis and/or
	cardiov	cardiovascularization.
	Highly	Highly preferred indications
	include	include antiangiogenic activity
	to treat	to treat solid tumors,
	leukem	leukemias, and Kaposi"s
	sarcom	sarcoma, and retinal disorders.

Highly preferred indications
 include neoplasms and cancer,
such as, Kaposi"s sarcoma,
hemangioma (capillary and
cavernous), glomus tumors,
telangiectasia, bacillary
angiomatosis,
hemangioendothelioma,
angiosarcoma,
haemangiopericytoma,
lymphangioma,
lymphangiosarcoma. Highly
preferred indications also
include cancers such as,
prostate, breast, lung, colon,
pancreatic, esophageal,
stomach, brain, liver, and
urinary cancer. Preferred
indications include benign
dysproliferative disorders and
pre-neoplastic conditions, such
as, for example, hyperplasia,
metaplasia, and/or dysplasia.
Highly preferred indications
 also include arterial disease,
such as, atherosclerosis,
hypertension, coronary artery
disease, inflammatory
vasculitides, Reynaud's
disease and Reynaud"s
phenomenom, aneurysms,

			restenosis: venous and
-			
			lymphatic disorders such as
			thrombophlebitis,
			lymphangitis, and
			lymphedema; and other
			vascular disorders such as
			peripheral vascular disease,
			and cancer. Highly
			preferred indications also
			include trauma such as
			wounds, burns, and injured
			tissue (e.g., vascular injury
			such as, injury resulting from
			balloon angioplasty, and
		-	atheroschlerotic lesions),
			implant fixation, scarring,
			ischemia reperfusion injury,
			rheumatoid arthritis,
			cerebrovascular disease, renal
			diseases such as acute renal
			failure, and osteoporosis.
			Additional highly preferred
			indications include stroke,
		 	graft rejection, diabetic or
			other retinopathies, thrombotic
			and coagulative disorders,
			vascularitis, lymph
			angiogenesis, sexual disorders,
			age-related macular
		 	degeneration, and treatment
			/prevention of endometriosis

					and related conditions.
					Additional highly preferred
					indications include fibromas,
					heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease.
					Preferred indications include
					blood disorders (e.g., as
					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HRDFD27	1421	Activation of	Assays for the activation of	Highly preferred indications
473			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.

	response element in	well-known in the art and may	Highly preferred indications
	immune cells (such	be used or routinely modified	include blood disorders (e.g.,
	as natural killer	to assess the ability of	as described below under
 -	cells).	polypeptides of the invention	"Immune Activity", "Blood-
		(including antibodies and	Related Disorders", and/or
		agonists or antagonists of the	"Cardiovascular Disorders").
		invention) to regulate NFKB	Highly preferred indications
		transcription factors and	include autoimmune diseases
 		modulate expression of	(e.g., rheumatoid arthritis,
		immunomodulatory genes.	systemic lupus erythematosis,
 		Exemplary assays for	multiple sclerosis and/or as
		transcription through the	described below), and
		NFKB response element that	immunodeficiencies (e.g., as
		may be used or rountinely	described below). An
 		modified to test NFKB-	additional highly preferred
		response element activity of	indication is infection (e.g.,
		polypeptides of the invention	AIDS, and/or an infectious
 		(including antibodies and	disease as described below
 		agonists or antagonists of the	under "Infectious Disease").
 		invention) include assays	Highly preferred indications
		disclosed in Berger et al., Gene	include neoplastic diseases
		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
 		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Valle	Disorders"). Highly preferred
		Blazquez et al, Immunology	indications include neoplasms
		90(3):455-460 (1997);	and cancers, such as, for
		Aramburau et al., J Exp Med	example, melanoma, renal cell
 		82(3):801-810 (1995); and	carcinoma, leukemia,
		Fraser et al., 29(3):838-844	lymphoma, and prostate,

				(1999), the contents of each of which are herein incorporated	breast, lung, colon, pancreatic, esophageal, stomach, brain,
				by reference in its entirety.  NK cells that may be used	liver and urinary cancer. Other preferred indications include
				according to these assays are	benign dysproliferative
				publicly available (e.g., through the ATCC).	disorders and pre-neoplastic conditions, such as, for
				Exemplary human NK cells	example, hyperplasia,
				that may be used according to	metaplasia, and/or dysplasia.
				these assays include the NKL	Preferred indications also
				cell line, which is a human natural killer cell line	include anemia, pancytopenia, leukonenia, thrombocytopenia,
				established from the peripheral	Hodgkin's disease, acute
				blood of a patient with large	lymphocytic anemia (ALL),
				granular lymphocytic	plasmacytomas, multiple
				leukemia. This IL-2 dependent	myeloma, Burkitt's lymphoma,
				suspension culture cell line has	arthritis, AIDS, granulomatous
				a morphology resembling that	disease, inflammatory bowel
				of activated NK cells.	disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
474	HROAJ03	1422	IL-4 in HMC		
	HROAJ03	1422	Activation of	Kinase assay. JNK and p38	A highly preferred
474			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for

Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
•	apoptosis are well known in	growth. An alternative highly
	the art and may be used or	preferred embodiment of the
	routinely modified to assess	invention includes a method
	the ability of polypeptides of	for inhibiting endothelial cell
	the invention (including	growth. A highly preferred
	antibodies and agonists or	embodiment of the invention
	antagonists of the invention) to	includes a method for
	promote or inhibit cell	stimulating endothelial cell
	proliferation, activation, and	proliferation. An alternative
	apoptosis. Exemplary assays	highly preferred embodiment
	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
	assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention

includes a method for				A highly preferred		g to includes a method for	n stimulating angiogenisis. An	ells	embodiment of the invention	e includes a method for	are inhibiting angiogenesis. A	highly preferred embodiment		method for reducing cardiac		tion.   highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	reouroitation left ventricular
reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.				-										
																													-	
																								-						

dysfunction atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	

include neoplasms and cancer,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and
		-				~		-						-		-										-			

	Imphatio disorders such as
 	iyinpilane disolderis sucii as
	thrombophlebitis,
	lymphangitis, and
	lymphedema; and other
	vascular disorders such as
	peripheral vascular disease,
	and cancer. Highly
	preferred indications also
	include trauma such as
	wounds, burns, and injured
 	tissue (e.g., vascular injury
	such as, injury resulting from
	balloon angioplasty, and
	atheroschlerotic lesions),
	implant fixation, scarring,
	ischemia reperfusion injury,
	rheumatoid arthritis,
	cerebrovascular disease, renal
 	diseases such as acute renal
 	failure, and osteoporosis.
	Additional highly preferred
	indications include stroke,
 	graft rejection, diabetic or
	other retinopathies, thrombotic
	and coagulative disorders,
 	vascularitis, lymph
 	angiogenesis, sexual disorders,
	age-related macular
	degeneration, and treatment
	/prevention of endometriosis
	and related conditions.

					Additional highly preferred
					indications include fibromas,
					heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease.
					Preferred indications include
					blood disorders (e.g., as
					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
,					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HRTAE58	1423	Production of TNF	TNFa FMAT. Assays for	A highly preferred
475			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)

fibroblasts, smooth muscle, and other cell types that exert a wide variety of cinflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J	TNF alpha production. An	alternative highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.
	fibroblasts, smooth muscle,	and other cell types that exert a	wide variety of inflammatory	and cytotoxic effects on a	variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-
																												-			

	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases
	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); Verhasselt et al., Eur J	and/or as described below
	Immunol 28(11):3886-3890	under "Hyperproliferative
	(1198); Dahlen et al., J	Disorders"). Additionally,
	Immunol 160(7):3585-3593	highly preferred indications
	(1998); Verhasselt et al., J	include neoplasms and
	Immunol 158:2919-2925	cancers, such as, leukemia,
	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
	(1999), the contents of each of	tumors, and prostate, breast,
	which are herein incorporated	lung, colon, pancreatic,
	by reference in its entirety.	esophageal, stomach, brain,
	Human dendritic cells that may	liver and urinary cancer. Other
	be used according to these	preferred indications include
	assays may be isolated using	benign dysproliferative
	techniques disclosed herein or	disorders and pre-neoplastic
	otherwise known in the art.	conditions, such as, for
	Human dendritic cells are	example, hyperplasia,
	antigen presenting cells in	metaplasia, and/or dysplasia.
	suspension culture, which,	Preferred indications include
	when activated by antigen	anemia, pancytopenia,
	and/or cytokines, initiate and	leukopenia, thrombocytopenia,
	upregulate T cell proliferation	Hodgkin's disease, acute
	and functional activities.	lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
	!	disease, neutropenia,

neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours.  LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of
	Activation of Transcription
	1423
	HRTAE58
	475

				specific tumoral markers in colon cancer. See, Patan et al., Circ Res, 89(8):732-39 (2001), the contents of which are berein incompared by	
				reference in its entirety.	
	HSATR82	1424	Activation of	Assays for the activation of	A preferred embodiment of
476			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated

					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
	-				reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
	_				asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
!	:			!	under "Infectious Disease").
	HSAUK57	1425	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
477				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a

	II6 induces extotoxic T cells.	method for inhibiting (e.g.,
	Deregulated expression of IL-6	reducing) IL-6 production. A
	has been linked to autoimmune	highly preferrred indication is
	disease, plasmacytomas,	the stimulation or enhancement
	myelomas, and chronic	of mucosal immunity. Highly
	hyperproliferative diseases.	preferred indications include
	Assays for immunomodulatory	blood disorders (e.g., as
	and differentiation factor	described below under
	proteins produced by a large	"Immune Activity", "Blood-
	variety of cells where the	Related Disorders", and/or
	expression level is strongly	"Cardiovascular Disorders"),
	regulated by cytokines, growth	and infection (e.g., as
	factors, and hormones are well	described below under
	known in the art and may be	"Infectious Disease"). Highly
	used or routinely modified to	preferred indications include
	assess the ability of	autoimmune diseases (e.g.,
	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory

	may be used or routinely	disorders. Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	when activated by antigen	leukopenia, thrombocytopenia,
	and/or cytokines, initiate and	Hodgkin's disease, acute
	upregulate T cell proliferation	lymphocytic anemia (ALL),
	and functional activities.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,

granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing)  TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing)  TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-
		TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or
	IgG in Human B cells SAC	Production of TNF alpha by dendritic cells
	1425	1426
	HSAUK57	HSAUL82
	477	478

	antagonists of the invention) to	Related Disorders", and/or
	mediate immunomodulation,	
	modulate inflammation and	Highly preferred indications
	cytotoxicity. Exemplary	include autoimmune diseases
	assays that test for	(e.g., rheumatoid arthritis,
	immunomodulatory proteins	systemic lupus erythematosis,
	evaluate the production of	Crohn"s disease, multiple
	cytokines such as tumor	sclerosis and/or as described
	necrosis factor alpha (TNFa),	below), immunodeficiencies
	and the induction or inhibition	(e.g., as described below),
	of an inflammatory or	boosting a T cell-mediated
	cytotoxic response. Such	immune response, and
	assays that may be used or	suppressing a T cell-mediated
	routinely modified to test	immune response. Additional
	immunomodulatory activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders, and
	agonists or antagonists of the	treating joint damage in
***************************************	invention) include assays	patients with rheumatoid
	disclosed in Miraglia et al., J	arthritis. An additional highly
	Biomolecular Screening 4:193-	
	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases
	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); Verhasselt et al., Eur J	and/or as described below
	Immunol 28(11):3886-3890	under "Hyperproliferative
	(1198); Dahlen et al., J	Disorders"). Additionally,
	Immunol 160(7):3585-3593	highly preferred indications
	(1998); Verhasselt et al., J	include neoplasms and
	Immunol 158:2919-2925	cancers, such as, leukemia,
	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma

8 (e.g., malignant glioma), solid	och of	_	esophageal, stomach, brain,		sse preferred indications include	using benign dysproliferative	rein or disorders and pre-neoplastic	art. conditions, such as, for	re example, hyperplasia,	in metaplasia, and/or dysplasia.	ch, Preferred indications include	en anemia, pancytopenia,	pur	ration Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication
Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.															

					is infection (e.g., an infectious disease as described below under "Infectious Disease").
478	HSAUL82	1426	Activation of transcription through NFKB response element in immune cells (such as basophils).	This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications include immunological and hempatopoictic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"). Preferred indications also include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described
				disclosed in Berger et al., Gene	below under

				66:1-10 (1998); Cullen and	"Hyperproliferative
				Maim, Methods in Enzymoi 216:362-368 (1992); Henthorn	Disorders ). Preferred indications include neoplasms
				et al., Proc Natl Acad Sci USA	and cancer, such as, for
				85:6342-6346 (1988); Marone	example, leukemia, lymphoma,
				et al, Int Arch Allergy	melanoma, and prostate,
				Immunol 114(3):207-17	breast, lung, colon, pancreatic,
_				(1997), the contents of each of	esophageal, stomach, brain,
				which are herein incorporated	liver, urinary tract cancers and
				by reference in its entirety.	as described below under
				Basophils that may be used	"Hyperproliferative
				according to these assays are	Disorders".
				publicly available (e.g.,	
				through the ATCC).	
				Exemplary human basophil	
				cell lines that may be used	
				according to these assays	
				include Ku812, originally	
				established from a patient with	
				chronic myelogenous	
				leukemia. It is an immature	
				prebasophilic cell line that can	
				be induced to differentiate into	
				mature basophils.	
	HSAVH65	1427	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
479			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",

the ability of polypeptides of	"Cardiovascular Disorders".
the invention (including	and/or "Blood-Related
antibodies and agonists or	Disorders"), and infection
antagonists of the invention) to	(e.g., an infectious disease as
promote or inhibit immune cell	described below under
(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
activation, and apoptosis.	preferred indications include
Exemplary assays for JNK and	autoimmune diseases (e.g.,
p38 kinase activity that may be	rheumatoid arthritis, systemic
used or routinely modified to	lupus erythematosis, multiple
test JNK and p38 kinase-	sclerosis and/or as described
induced activity of	below) and
polypeptides of the invention	immunodeficiencies (e.g., as
(including antibodies and	described below). Additional
agonists or antagonists of the	highly preferred indications
invention) include the assays	include inflammation and
disclosed in Forrer et al., Biol	inflammatory disorders.
Chem 379(8-9):1101-1110	Highly preferred indications
(1998); Gupta et al., Exp Cell	also include neoplastic
Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
Kyriakis JM, Biochem Soc	lymphoma, and/or as described
Symp 64:29-48 (1999); Chang	below under
and Karin, Nature	"Hyperproliferative
410(6824):37-40 (2001); and	Disorders"). Highly preferred
Cobb MH, Prog Biophys Mol	indications include neoplasms
Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
the contents of each of which	lymphoma, prostate, breast,
are herein incorporated by	lung, colon, pancreatic,
reference in its entirety. T	esophageal, stomach, brain,
cells that may be used	liver, and urinary cancer. Other
according to these assays are	preferred indications include

				publicly available (e.g., through the ATCC).  Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic	benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, alleroy, anemia, nanoytonenia
				activity.	leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease.
					inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
479	HSAVH65	1427	ICAM in Normal Human Bronchial Epitheliae		
479	HSAVH65	1427	IL-8 in Normal Human Bronchial Epitheliae		
480	HSAVK10	1428	Activation of transcription through AP1 response element in	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative
			immune cells (such	routinely modified to assess	Disorders"), blood disorders

	as T-cells).	the ability of polypeptides of	(e.g., as described below under
	`	the invention (including	"Immune Activity",
		antibodies and agonists or	"Cardiovascular Disorders",
		antagonists of the invention) to	and/or "Blood-Related
		modulate growth and other cell	Disorders"), and infection
		functions. Exemplary assays	(e.g., an infectious disease as
		for transcription through the	described below under
		AP1 response element that	"Infectious Disease"). Highly
		may be used or routinely	preferred indications include
		modified to test AP1-response	autoimmune diseases (e.g.,
		element activity of	rheumatoid arthritis, systemic
		polypeptides of the invention	lupus erythematosis, multiple
		(including antibodies and	sclerosis and/or as described
		agonists or antagonists of the	below) and
		invention) include assays	immunodeficiencies (e.g., as
		disclosed in Berger et al., Gene	described below). Additional
		66:1-10 (1988); Cullen and	highly preferred indications
		Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
		et al., Proc Natl Acad Sci USA	Highly preferred indications
		85:6342-6346 (1988);	also include neoplastic
		Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
		272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
		18(9):4986-4993 (1998); and	"Hyperproliferative
_		Fraser et al., Eur J Immunol	Disorders"). Highly preferred
		29(3):838-844 (1999), the	indications include neoplasms
		contents of each of which are	and cancers, such as, leukemia,
		herein incorporated by	lymphoma, prostate, breast,
		reference in its entirety. T	lung, colon, pancreatic,
		cells that may be used	esophageal, stomach, brain,

				according to these assays are	liver, and urinary cancer. Other
				publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary mouse T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the CTLL cell	example, hyperplasia,
				line, which is an IL-2	metaplasia, and/or dysplasia.
	_			dependent suspension-culture	Preferred indications include
				cell line with cytotoxic	arthritis, asthma, AIDS,
				activity.	allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HSAVK10	1428	Activation of	Assays for the activation of	Preferred indications include
480			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious

ıli	invention) to increase cAMP	Disease"). Preferred
and	and regulate CREB	indications include
trai	transcription factors, and	autoimmune diseases (e.g.,
om	modulate expression of genes	rheumatoid arthritis, systemic
nui	involved in a wide variety of	lupus erythematosis, multiple
leo leo	cell functions. Exemplary	sclerosis and/or as described
ass	assays for transcription	below), immunodeficiencies
thr	through the cAMP response	(e.g., as described below),
ele	element that may be used or	boosting a T cell-mediated
10.1	routinely modified to test	immune response, and
CA	cAMP-response element	suppressing a T cell-mediated
act	activity of polypeptides of the	immune response. Additional
ni	invention (including antibodies	preferred indications include
and	and agonists or antagonists of	inflammation and
the	the invention) include assays	inflammatory disorders.
dis	disclosed in Berger et al., Gene	Highly preferred indications
99	66:1-10 (1998); Cullen and	include neoplastic diseases
Mg	Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
210	216:362-368 (1992); Henthorn	and/or as described below
et 5	et al., Proc Natl Acad Sci USA	under "Hyperproliferative
855	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
al.,	al., Virus Genes 15(2):105-117	indications include neoplasms
(15)	(1997); and Belkowski et al., J	and cancers, such as, for
lm Im	Immunol 161(2):659-665	example, leukemia, lymphoma
(15)	(1998), the contents of each of	(e.g., T cell lymphoma,
l wh	which are herein incorporated	Burkitt's lymphoma, non-
by	by reference in its entirety. T	Hodgkins lymphoma,
[cel	cells that may be used	Hodgkin"s disease),
300	according to these assays are	melanoma, and prostate,
[nd]	publicly available (e.g.,	breast, lung, colon, pancreatic,
thr	through the ATCC).	esophageal, stomach, brain,

				Exemplary mouse I cells that	liver and urinary cancer. Other
				may be used according to these	preferred indications include
				assays include the CTLL cell	benign dysproliferative
				line, which is a suspension	disorders and pre-neoplastic
				culture of IL-2 dependent	conditions, such as, for
				cytotoxic T cells.	example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HSAVK10	1428	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
480				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a

IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
Deregulated expression of IL-6	reducing) IL-6 production. A
has been linked to autoimmune	highly preferrred indication is
disease, plasmacytomas,	the stimulation or enhancement
myelomas, and chronic	of mucosal immunity. Highly
hyperproliferative diseases.	preferred indications include
Assays for immunomodulatory	blood disorders (e.g., as
and differentiation factor	described below under
proteins produced by a large	"Immune Activity", "Blood-
variety of cells where the	Related Disorders", and/or
expression level is strongly	"Cardiovascular Disorders"),
regulated by cytokines, growth	and infection (e.g., as
factors, and hormones are well	described below under
known in the art and may be	"Infectious Disease"). Highly
used or routinely modified to	preferred indications include
assess the ability of	autoimmune diseases (e.g.,
polypeptides of the invention	rheumatoid arthritis, systemic
(including antibodies and	lupus erythematosis, multiple
agonists or antagonists of the	sclerosis and/or as described
invention) to mediate	below) and
immunomodulation and	immunodeficiencies (e.g., as
 differentiation and modulate T	described below). Highly
cell proliferation and function.	preferred indications also
Exemplary assays that test for	include boosting a B cell-
immunomodulatory proteins	mediated immune response
evaluate the production of	and alternatively suppressing a
cytokines, such as IL-6, and	B cell-mediated immune
the stimulation and	response. Highly preferred
upregulation of T cell	indications include
proliferation and functional	inflammation and
activities. Such assays that	inflammatory

		may be used or routinely	disorders. Additional highly
 		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
		polypeptides of the invention	neoplastic diseases (e.g.,
		(including antibodies and	myeloma, plasmacytoma,
 		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
-		disclosed in Miraglia et al., J	below under
 		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
	_	"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
_		Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
		which are herein incorporated	pancreatic, esophageal,
		by reference in its entirety.	stomach, brain, liver and
		Human dendritic cells that may	urinary cancer. Other preferred
_		be used according to these	indications include benign
		assays may be isolated using	dysproliferative disorders and
-		techniques disclosed herein or	pre-neoplastic conditions, such
		otherwise known in the art.	as, for example, hyperplasia,
		Human dendritic cells are	metaplasia, and/or dysplasia.
		antigen presenting cells in	Preferred indications include
		suspension culture, which,	anemia, pancytopenia,
 		when activated by antigen	leukopenia, thrombocytopenia,
		and/or cytokines, initiate and	Hodgkin's disease, acute
		upregulate T cell proliferation	lymphocytic anemia (ALL),
		and functional activities.	multiple myeloma, Burkitt's
			lymphoma, arthritis, AIDS,

		,			granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
480	HSAVK10	1428	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under

assavs that test for	"Immune Activity", "Blood-
immunomodulatory proteins	Related Disorders", and/or
evaluate the production of	"Cardiovascular Disorders").
chemokines, such as	Highly preferred indications
macrophage inflammatory	include autoimmune diseases
protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
the activation of	systemic lupus erythematosis,
monocytes/macrophages and T	multiple sclerosis and/or as
cells. Such assays that may be	described below) and
used or routinely modified to	immunodeficiencies (e.g., as
test immunomodulatory and	described below). Additional
 chemotaxis activity of	highly preferred indications
polypeptides of the invention	include inflammation and
 (including antibodies and	inflammatory disorders.
agonists or antagonists of the	Preferred indications also
invention) include assays	include anemia, pancytopenia,
disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
Biomolecular Screening 4:193-	Hodgkin's disease, acute
204(1999); Rowland et al.,	lymphocytic anemia (ALL),
"Lymphocytes: a practical	plasmacytomas, multiple
approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,
(2000); Satthaporn and	arthritis, AIDS, granulomatous
Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
29 (2000); Verhasselt et al., J	suppression of immune
Immunol 158:2919-2925	reactions to transplanted
 (1997); and Nardelli et al., J	organs and tissues, hemophilia,
Leukoc Biol 65:822-828	hypercoagulation, diabetes
(1999), the contents of each of	mellitus, endocarditis,
which are herein incorporated	meningitis, Lyme Disease,

				by reference in its entirety.  Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.  Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	asthma, and allergy.  Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic
	HSAVK10	1428	SEAP in		example, hyperplasia, metaplasia, and/or dysplasia.
480	HSAWD74	1429	Senescence Assay Regulation of transcription via	Assays for the regulation of transcription through the	A highly preferred indication is diabetes mellitus.
			element in adipocytes and preadipocytes	well-known in the art and may be used or routinely modified to assess the ability of	indications include complications associated with diabetes (e.g., diabetic
				polypeptides of the invention (including antibodies and agonists or antagonists of the	retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure,
				invention) to activate the	nephropathy and/or other

DMEF1 response element in a	diseases and disorders as
reporter construct (such as that	described in the "Renal
containing the GLUT4	Disorders" section below),
promoter) and to regulate	diabetic neuropathy, nerve
insulin production. The	disease and nerve damage
DMEF1 response element is	(e.g., due to diabetic
present in the GLUT4	neuropathy), blood vessel
promoter and binds to MEF2	blockage, heart disease, stroke,
transcription factor and another	impotence (e.g., due to diabetic
transcription factor that is	neuropathy or blood vessel
required for insulin regulation	blockage), seizures, mental
of Glut4 expression in skeletal	confusion, drowsiness,
muscle. GLUT4 is the primary	nonketotic hyperglycemic-
insulin-responsive glucose	hyperosmolar coma,
transporter in fat and muscle	cardiovascular disease (e.g.,
 tissue. Exemplary assays that	heart disease, atherosclerosis,
may be used or routinely	microvascular disease,
modified to test for DMEF1	hypertension, stroke, and other
response element activity (in	diseases and disorders as
adipocytes and pre-adipocytes)	described in the
by polypeptides of the	"Cardiovascular Disorders"
invention (including antibodies	section below), dyslipidemia,
and agonists or antagonists of	endocrine disorders (as
the invention) include assays	described in the "Endocrine
 disclosed inThai, M.V., et al., J	Disorders" section below),
Biol Chem, 273(23):14285-92	neuropathy, vision impairment
(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
Chem, 275(21):16323-8	blindness), ulcers and impaired
(2000); Liu, M.L., et al., J Biol	wound healing, and infection
Chem, 269(45):28514-21	(e.g., infectious diseases and
(1994); "Identification of a 30-	disorders as described in the

<u>а</u>	base pair regulatory element and novel DNA binding	"Infectious Diseases" section below, especially of the
<u>a</u> .	protein that regulates the	urinary tract and skin). An
<del>1</del> <del>1</del>	transgenic mice", J Biol Chem.	additional inguity preferred indication is obesity and/or
2	2000 Aug 4;275(31):23666-73;	complications associated with
 H	Berger, et al., Gene 66:1-10	obesity. Additional highly
	(1988); and, Cullen, B., et al.,	preferred indications include
_	Methods in Enzymol.	weight loss or alternatively,
 2	216:362–368 (1992), the	weight gain. Additional highly
3	contents of each of which is	preferred indications are
h h	herein incorporated by	complications associated with
). I	reference in its entirety.	insulin resistance.
 4	Adipocytes and pre-adipocytes	
#	that may be used according to	
<del></del>	these assays are publicly	
В	available (e.g., through the	
<u> </u>	ATCC) and/or may be	
2	routinely generated.	
<u> </u>	Exemplary cells that may be	
n	used according to these assays	
 .=	include the mouse 3T3-L1 cell	
	line which is an adherent	
u	mouse preadipocyte cell line.	
	Mouse 3T3-L1 cells are a	
	continuous substrain of 3T3	
 9	fibroblasts developed through	
3	clonal isolation. These cells	
 n	undergo a pre-adipocyte to	
B	adipose-like conversion under	
8	appropriate differentiation	

				culture conditions.	
	HSAWD74	1429	Activation of	This reporter assay measures	Highly preferred indications
481			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
·				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
_				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
		-		modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
-				Exemplary assays for	indications include neoplastic
				transcription through the	diseases (e.g., leukemia,
			-	NFAT response element that	lymphoma, melanoma,
				may be used or routinely	prostate, breast, lung, colon,
				modified to test NFAT-	pancreatic, esophageal,
				response element activity of	stomach, brain, liver, and
				polypeptides of the invention	urinary tract cancers and/or as

		(including antibodies and	described helow under
		agonists or antagonists of the	"Hyperproliferative
		invention) include assays	Disorders"). Other preferred
-		disclosed in Berger et al., Gene	indications include benign
		66:1-10 (1998); Cullen and	dysproliferative disorders and
-		Malm, Methods in Enzymol	pre-neoplastic conditions, such
		216:362-368 (1992); Henthorn	as, for example, hyperplasia,
-		et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
		85:6342-6346 (1988); De Boer	Preferred indications include
		et al., Int J Biochem Cell Biol	anemia, pancytopenia,
		31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
		et al., J Immunol	leukemias, Hodgkin's disease,
		165(12):7215-7223 (2000);	acute lymphocytic anemia
		Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
		16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
		al., J Exp Med 188:527-537	granulomatous disease,
		(1998), the contents of each of	inflammatory bowel disease,
		which are herein incorporated	sepsis, neutropenia,
		by reference in its entirety.	neutrophilia, psoriasis,
		Mast cells that may be used	suppression of immune
		according to these assays are	reactions to transplanted
		publicly available (e.g.,	organs and tissues, hemophilia,
		through the ATCC).	hypercoagulation, diabetes
		Exemplary human mast cells	mellitus, endocarditis,
	-	that may be used according to	meningitis, and Lyme Disease.
	-	these assays include the HMC-	
		1 cell line, which is an	
		immature human mast cell line	
		established from the peripheral	
		blood of a patient with mast	

cell leukemia, and exhibits many characteristics of immature mast cells.	adipose cells (such increases or decreases) of as 3T3-L1 cells) viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the Cell Titler-Gloó Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells in collain. Calls
	1429
	HSAWD74
	481

				adipose-like state before being	
				used in the screen. See Green H and Meuth M. Cell 3: 127-	
				133 (1974), which is herein	
				incorporated by reference in its	
				entirety.	
482	HSAWZ41	1430	SEAP in 293/ISRE		
	HSAWZ41	1430	Activation of	Assays for the activation of	A highly preferred indication
482			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,

binding sequence for the	impotence (e.g., due to diabetic
transcription factor CREB	neuropathy or blood vessel
(CRE binding protein).	blockage), seizures, mental
Exemplary assays for	confusion, drowsiness,
transcription through the	nonketotic hyperglycemic-
cAMP response element that	hyperosmolar coma,
may be used or routinely	cardiovascular disease (e.g.,
modified to test cAMP-	heart disease, atherosclerosis,
response element activity of	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in Berger et al., Gene	section below), dyslipidemia,
66:1-10 (1998); Cullen and	endocrine disorders (as
Malm, Methods in Enzymol	described in the "Endocrine
216:362-368 (1992); Henthorn	Disorders" section below),
et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
et al., Mol Cell Biol	blindness), ulcers and impaired
20(3):1008-1020 (2000); and	wound healing, and infection
 Klemm et al., J Biol Chem	(e.g., infectious diseases and
273:917-923 (1998), the	disorders as described in the
contents of each of which are	"Infectious Diseases" section
herein incorporated by	below, especially of the
reference in its entirety. Pre-	urinary tract and skin), carpal
adipocytes that may be used	tunnel syndrome and
according to these assays are	Dupuytren's contracture).
publicly available (e.g.,	Additional highly preferred
through the ATCC) and/or	indications are complications
may be routinely generated.	associated with insulin

			Exemplary mouse adipocyte	resistance.
			cells that may be used	
			according to these assays	
			is an adherent mouse	
			preadipocyte cell line that is a	
			continuous substrain of 3T3	
			fibroblast cells developed	
			through clonal isolation and	
			undergo a pre-adipocyte to	
			adipose-like conversion under	
		- · · · -	appropriate differentiation	
			conditions known in the art.	
HSAWZ41	1430	Activation of	Assays for the activation of	Preferred indications
		transcription	transcription through the AP1	include neoplastic diseases
		through AP1	response element are known in	(e.g., as described below under
		response element in	the art and may be used or	"Hyperproliferative
		immune cells (such	routinely modified to assess	Disorders"), blood disorders
		as T-cells).	the ability of polypeptides of	(e.g., as described below under
			the invention (including	"Immune Activity",
			antibodies and agonists or	"Cardiovascular Disorders",
			antagonists of the invention) to	and/or "Blood-Related
			modulate growth and other cell	Disorders"), and infection
			functions. Exemplary assays	(e.g., an infectious disease as
			for transcription through the	described below under
			AP1 response element that	"Infectious Disease"). Highly
			may be used or routinely	preferred indications include
			modified to test AP1-response	autoimmune diseases (e.g.,
			element activity of	rheumatoid arthritis, systemic
			polypeptides of the invention	lupus erythematosis, multiple
			(including antibodies and	sclerosis and/or as described

agonists or antagonists of the		below) and
invention) include assays		immunodeficiencies (e.g., as
disclosed in Berger et al., Gene		described below). Additional
66:1-10 (1988); Cullen and		highly preferred indications
Malm, Methods in Enzymol		include inflammation and
216:362-368 (1992); Henthorn		inflammatory disorders.
et al., Proc Natl Acad Sci USA		Highly preferred indications
85:6342-6346 (1988);		also include neoplastic
Rellahan et al., J Biol Chem		diseases (e.g., leukemia,
272(49):30806-30811 (1997);		lymphoma, and/or as described
Chang et al., Mol Cell Biol		below under
18(9):4986-4993 (1998); and	- pı	"Hyperproliferative
Fraser et al., Eur J Immunol		Disorders"). Highly preferred
29(3):838-844 (1999), the		indications include neoplasms
contents of each of which are		and cancers, such as, leukemia,
herein incorporated by		lymphoma, prostate, breast,
reference in its entirety.	Ь	lung, colon, pancreatic,
cells that may be used		esophageal, stomach, brain,
according to these assays are		liver, and urinary cancer. Other
publicly available (e.g.,		preferred indications include
through the ATCC).		benign dysproliferative
Exemplary mouse T cells that		disorders and pre-neoplastic
may be used according to these	se	conditions, such as, for
assays include the CTLL cell		example, hyperplasia,
line, which is an IL-2		metaplasia, and/or dysplasia.
dependent suspension-culture	culture	Preferred indications include
cell line with cytotoxic		arthritis, asthma, AIDS,
activity.	<u></u>	allergy, anemia, pancytopenia,
	16	leukopenia, thrombocytopenia,
	<u> </u>	Hodgkin's disease, acute
	(1)	lymphocytic anemia (ALL),

					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
-					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HSAWZ41	1430	Activation of	Assays for the activation of	Highly preferred indications
482			transcription	transcription through the	include asthma, allergy,
			through NFKB	NFKB response element are	hypersensitivity reactions, and
			response element in	well-known in the art and may	inflammation. Preferred
			immune cells (such	be used or routinely modified	indications include infection
			as EOL1 cells).	to assess the ability of	(e.g., an infectious disease as
				polypeptides of the invention	described below under
				(including antibodies and	"Infectious Disease"),
				agonists or antagonists of the	immunological disorders,
	•			invention) to regulate NFKB	inflammation and
				transcription factors and	inflammatory disorders (e.g.,
				modulate expression of	as described below under
		- <del></del>		immunomodulatory genes.	"Immune Activity", and
				Exemplary assays for	"Blood-Related Disorders").
				transcription through the	Preferred indications include
				NFKB response element that	autoimmune diseases (e.g.,
				may be used or rountinely	rheumatoid arthritis, systemic
				modified to test NFKB-	lupus erythematosis, multiple
				response element activity of	sclerosis and/or as described
				polypeptides of the invention	below) and
				(including antibodies and	immunodeficiencies (e.g., as
		-		agonists or antagonists of the	described below).

invention) include assays disclosed in Berger et al., Gene 66.1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al., Immunology 90(3):455-460 (1987); Aramburau et al., J Exp Med 82(3):455-460 (1997); Aramburau et al., 1989), and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. For example, a reporter assay (which measures increases in transcription inducible from a NFKB responsive element in EOL-1 cells) may link the NFKB element to a reporter gene and binds to the NFKB transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils				
	invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle	Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated	by reference in its entirety. For example, a reporter assay (which measures increases in transcription inducible from a NFkB responsive element in EOL-1 cells) may link the NFKB element to a repeorter gene and binds to the NFKB transcription factor which is	upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important

through the GATA3 response	indications include neoplastic
element that may be used or	diseases (e.g., leukemia,
routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
activity of polypeptides of the	pancreatic, esophageal,
invention (including antibodies	stomach, brain, liver, and
and agonists or antagonists of	urinary tract cancers and/or as
the invention) include assays	described below under
disclosed in Berger et al., Gene	"Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);	Preferred indications include
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
contents of each of which are	lymphoma, arthritis, AIDS,
herein incorporated by	granulomatous disease,
reference in its entirety. Mast	inflammatory bowel disease,
cells that may be used	sepsis, neutropenia,
according to these assays are	neutrophilia, psoriasis,
publicly available (e.g.,	suppression of immune
through the ATCC).	reactions to transplanted
Exemplary human mast cells	organs and tissues, hemophilia,
that may be used according to	hypercoagulation, diabetes

				e HMC-	mellitus, endocarditis,
				immature human mast cell line	mennigms, and Lyme Disease.
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HSAWZ41	1430	Activation of	This reporter assay measures	Highly preferred indications
482			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred

Exemplary assays for	indications include neoplastic
transcription through the	diseases (e.g., leukemia,
NFAT response element that	lymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
(including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
 216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
 et al., J Immunol	leukemias, Hodgkin's disease,
 165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
al., J Exp Med 188:527-537	granulomatous disease,
(1998), the contents of each of	inflammatory bowel disease,
which are herein incorporated	sepsis, neutropenia,
by reference in its entirety.	neutrophilia, psoriasis,
Mast cells that may be used	suppression of immune
according to these assays are	reactions to transplanted
publicly available (e.g.,	organs and tissues, hemophilia,
through the ATCC).	hypercoagulation, diabetes

				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HSAWZ41	1430	Activation of	Assays for the activation of	A preferred embodiment of
482			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple

	invention (including antibodies	sclerosis and/or as described
	and agonists or antagonists of	below), immunodeficiencies
	the invention) include assays	(e.g., as described below),
	disclosed in Berger et al., Gene	boosting a T cell-mediated
	66:1-10 (1998); Cullen and	immune response, and
	Malm, Methods in Enzymol	suppressing a T cell-mediated
	216:362-368 (1992); Henthorn	immune response. Additional
	et al., Proc Natl Acad Sci USA	highly preferred indications
	85:6342-6346 (1988); Benson	include inflammation and
	et al., J Immunol 153(9):3862-	inflammatory disorders, and
	3873 (1994); and Black et al.,	treating joint damage in
	Virus Genes 12(2):105-117	patients with rheumatoid
	(1997), the content of each of	arthritis. An additional highly
	which are herein incorporated	preferred indication is sepsis.
	by reference in its entirety. T	Highly preferred indications
	cells that may be used	include neoplastic diseases
	according to these assays are	(e.g., leukemia, lymphoma,
	publicly available (e.g.,	and/or as described below
	through the ATCC).	under "Hyperproliferative
	Exemplary T cells that may be	Disorders"). Additionally,
	used according to these assays	highly preferred indications
	include the NK-YT cell line,	include neoplasms and
	which is a human natural killer	cancers, such as, for example,
	 cell line with cytolytic and	leukemia, lymphoma,
	cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include

					henion dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
482	HSAWZ41	1430	SEAP in OE-21		
	HSAWZ41	1430	Activation of	Assays for the activation of	Highly preferred indications

482		transcription	transcription through the	include neoplastic diseases
		through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
		response element in	Site (GAS) response element	and/or as described below
		immune cells (such	are well-known in the art and	under "Hyperproliferative
		as T-cells).	may be used or routinely	Disorders"). Highly preferred
-			modified to assess the ability	indications include neoplasms
			of polypeptides of the	and cancers, such as, for
			invention (including antibodies	example, leukemia, lymphoma
			and agonists or antagonists of	(e.g., T cell lymphoma,
			the invention) to regulate	Burkitt's lymphoma, non-
			STAT transcription factors and	Hodgkins lymphoma,
			modulate gene expression	Hodgkin"s disease),
			involved in a wide variety of	melanoma, and prostate,
			cell functions. Exemplary	breast, lung, colon, pancreatic,
			assays for transcription	esophageal, stomach, brain,
			through the GAS response	liver and urinary cancer. Other
			element that may be used or	preferred indications include
			routinely modified to test	benign dysproliferative
			GAS-response element activity	disorders and pre-neoplastic
			of polypeptides of the	conditions, such as, for
			invention (including antibodies	example, hyperplasia,
	-		and agonists or antagonists of	metaplasia, and/or dysplasia.
			the invention) include assays	Preferred indications include
			disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
			66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
			Malm, Methods in Enzymol	lupus erythematosis, multiple
			216:362-368 (1992); Henthorn	sclerosis and/or as described
			et al., Proc Natl Acad Sci USA	below), immunodeficiencies
			85:6342-6346 (1988);	(e.g., as described below),
			Matikainen et al., Blood	boosting a T cell-mediated
			93(6):1980-1991 (1999); and	immune response, and

munol suppressing a T cell-mediated 1995), the immune response. Additional hich are preferred indications include	y inflammation and inflammatory disorders	ls,			ole	CC).   Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia.
Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are	herein incorporated by reference in its entirety	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).																					
														-													

					neutrophilia, psoriasis.
					suppression of immune
		-			reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HSAWZ41	1430	Activation of	Assays for the activation of	A highly preferred
482			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
			response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
			as T-cells).	well-known in the art and may	indications include
				be used or routinely modified	inflammation and
				to assess the ability of	inflammatory disorders.
				polypeptides of the invention	Preferred indications include
				(including antibodies and	blood disorders (e.g., as
				agonists or antagonists of the	described below under
				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
				modulate the expression of	"Cardiovascular Disorders").
				multiple genes. Exemplary	Preferred indications include
				assays for transcription	autoimmune diseases (e.g.,
				through the STAT6 response	rheumatoid arthritis, systemic
				element that may be used or	lupus erythematosis, multiple
				routinely modified to test	sclerosis and/or as described
				STAT6 response element	below) and
				activity of the polypeptides of	immunodeficiencies (e.g., as
				the invention (including	described below).
				antibodies and agonists or	Preferred indications include

antagonists of the invention)	neoplastic diseases (e.g.,
include assays disclosed in	leukemia, lymphoma,
Berger et al., Gene 66:1-10	melanoma, and/or as described
(1998); Cullen and Malm,	below under
Methods in Enzymol 216:362-	"Hyperproliferative
368 (1992); Henthorn et al.,	Disorders"). Preferred
Proc Natl Acad Sci USA	indications include neoplasms
85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
(1998); Moffatt et al.,	prostate, breast, lung, colon,
Transplantation 69(7):1521-	pancreatic, esophageal,
1523 (2000); Curiel et al., Eur	stomach, brain, liver and
J Immunol 27(8):1982-1987	urinary cancer. Other preferred
(1997); and Masuda et al., J	indications include benign
Biol Chem 275(38):29331-	dysproliferative disorders and
 29337 (2000), the contents of	pre-neoplastic conditions, such
each of which are herein	as, for example, hyperplasia,
incorporated by reference in its	metaplasia, and/or dysplasia.
entirety. T cells that may be	Preferred indications include
used according to these assays	anemia, pancytopenia,
are publicly available (e.g.,	leukopenia, thrombocytopenia,
through the ATCC).	Hodgkin's disease, acute
Exemplary T cells that may be	lymphocytic anemia (ALL),
used according to these assays	plasmacytomas, multiple
include the SUPT cell line,	myeloma, Burkitt's lymphoma,
which is a suspension culture	arthritis, AIDS, granulomatous
of IL-2 and IL-4 responsive T	disease, inflammatory bowel
cells.	disease, sepsis, neutropenia,
	neutrophilia, psoriasis,
	suppression of immune
	reactions to transplanted

					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred
					indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
483	HSAXA83	1431	Activation of transcription	Assays for the activation of transcription through the	A preferred embodiment of the invention includes a
			through serum response element in	Serum Response Element (SRE) are well-known in the	method for inhibiting (e.g., reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
	44-34		as 1-cens).	the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described

Dance of al Gons 66.1 10 holowy immunodofficionaise	(1998): Cullen and Malm. (e.g., as described below).	362-	 Proc Natl Acad Sci USA suppressing a T cell-mediated	p	Black et al., Virus Genes highly preferred indications	12(2):105-117 (1997), the   include inflammation and	content of each of which are inflammatory disorders, and	herein incorporated by treating joint damage in	reference in its entirety. T patients with rheumatoid	_	according to these assays are preferred indication is sepsis.	publicly available (e.g., Highly preferred indications	through the ATCC). include neoplastic diseases	Exemplary mouse T cells that (e.g., leukemia, lymphoma,	may be used according to these and/or as described below	LL cell	line, which is an IL-2 Disorders"). Additionally,	dependent suspension culture highly preferred indications	of T cells with cytotoxic include neoplasms and	activity. cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	nreferred indications include

			disorders and pre-neoplastic
			conditions, such as, for example, hyperplasia.
			metaplasia, and/or dysplasia.
-			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,
			meningitis, Lyme Disease,
			cardiac reperfusion injury, and
			asthma and allergy. An
			additional preferred indication
			is infection (e.g., an infectious
			disease as described below
			under "Infectious Disease").
1432	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
	Apoptosis	caspase apoptosis are well	embodiment of the invention
		known in the art and may be	includes a method for
		used or routinely modified to	stimulating endothelial cell

assess	assess the ability of	growth. An alternative highly
dolod	polypeptides of the invention	preferred embodiment of the
(inclu	(including antibodies and	invention includes a method
agoni	agonists or antagonists of the	for inhibiting endothelial cell
inven	invention) to promote caspase	growth. A highly preferred
protect	protease-mediated apoptosis.	embodiment of the invention
Induc	Induction of apoptosis in	includes a method for
endot	endothelial cells supporting the	stimulating endothelial cell
vascu	vasculature of tumors is	proliferation. An alternative
assoc	associated with tumor	highly preferred embodiment
regree	regression due to loss of tumor	of the invention includes a
poold	blood supply. Exemplary	method for inhibiting
assay	assays for caspase apoptosis	endothelial cell proliferation.
that n	that may be used or routinely	A highly preferred
modii	modified to test capase	embodiment of the invention
apopt	apoptosis activity of	includes a method for
polyp	polypeptides of the invention	stimulating apoptosis of
(inclu	(including antibodies and	endothelial cells. An
agoni	agonists or antagonists of the	alternative highly preferred
inven	invention) include the assays	embodiment of the invention
discle	disclosed in Lee et al., FEBS	includes a method for
Lett 4	Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
Nore	Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
209-2	209-218 (2000); and Karsan	A highly preferred
and H	and Harlan, J Atheroscler	embodiment of the invention
Thror	Thromb 3(2): 75-80 (1996);	includes a method for
the cc	the contents of each of which	stimulating angiogenisis. An
are he	are herein incorporated by	alternative highly preferred
refere	reference in its entirety.	embodiment of the invention
Endo	Endothelial cells that may be	includes a method for
psen	used according to these assays	inhibiting angiogenesis. A

nent	rs v	iac	ve	nent	B	iac	-	nde	as	-		l Jo s	_	estive	n,			ular	sis	lar	athy,	<u>ي</u>			and/or		rs").	ous		enic
embodir	includes	cing card	ı alternat	embodin	includes	cing card	Highly	tions incl	ses (e.g.,	' under	tive	l disorde	lar systen	ise, cong	pertensio		, valvula	ft ventric	erosclerc	otic vascu	nephrop	nt, cardia	vocardial	nic	verload,	ow under	Disorde	l indicati	ascular,	or angiog
highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic
highly	of the i	method	hyperti	highly	of the i	methoc	hyperti	preferr	neopla	describ	"Hype	Disord	the car	(e.g., h	heart fa	aortic s	cardion	regurgi	dysfun	and ath	disease	intraca	hyperti	infarct	hemod	as desc	"Cardi	Highly	include	endoth
.;e	rrces).	cells	ling to	vine		xample	ch line	ivolved	e, but			one,	asation.																	
ailable (	ercial so	lothelial	ed accore	clude bo	lial cells	n are an e	cells whi	and are ir	at includ	to,	vascular	ascular t	ell extrav																	
are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																	
are pu	throug	Exem	that m	these	aortic	(bAE	of enc	blood	in fun	are no	angio	perme	and in									_								
																											-			
												•					-							-	-		-			
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 	disorders (e.g., systemic
	disorders that affect vessels
	such as diabetes mellitus, as
	well as diseases of the vessels
	themselves, such as of the
	arteries, capillaries, veins
	and/or lymphatics). Highly
	 preferred are indications that
	stimulate angiogenesis and/or
	cardiovascularization. Highly
	preferred are indications that
	inhibit angiogenesis and/or
	cardiovascularization.
	Highly preferred indications
	include antiangiogenic activity
	to treat solid tumors,
	leukemias, and Kaposi"s
	sarcoma, and retinal disorders.
	Highly preferred indications
	include neoplasms and cancer,
	such as, Kaposi"s sarcoma,
	hemangioma (capillary and
	cavernous), glomus tumors,
	telangiectasia, bacillary
	angiomatosis,
	hemangioendothelioma,
	angiosarcoma,
	haemangiopericytoma,
	lymphangioma,
	lymphangiosarcoma. Highly

include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from
		-																												
				-										_				-												

balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring,	rheumatoid arthritis, cerebrovascular disease, renal	diseases such as acute renal failure, and osteoporosis. Additional highly preferred	indications include stroke, graft rejection, diabetic or	other retinopathies, thrombotic and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders, age-related macular	degeneration, and treatment	prevention of endometriosis and related conditions.	Additional highly preferred	indications include fibromas, heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include

					autoimmune diseases (e.g.,
					ineumatoru alumnis, systemie
					lupus erytnematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
-					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HSAYM40	1433	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
485				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
	-			Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-

	variety of cells where the	Related Disorders", and/or
	expression level is strongly	"Cardiovascular Disorders"),
	regulated by cytokines, growth	and infection (e.g., as
	factors, and hormones are well	described below under
	known in the art and may be	"Infectious Disease"). Highly
	used or routinely modified to	preferred indications include
	assess the ability of	autoimmune diseases (e.g.,
	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under

	Biomolecular Screening 4:193-204(1999): Rowland et al.	"Hyperproliferative Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	when activated by antigen	leukopenia, thrombocytopenia,
	and/or cytokines, initiate and	Hodgkin's disease, acute
	upregulate T cell proliferation	lymphocytic anemia (ALL),
	and functional activities.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,

					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
485	HSAYM40	1433	IgG in Human B cells SAC		
	HSAYM40	1433	Activation of	Assays for the activation of	A highly preferred
485			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
			response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
			as T-cells).	well-known in the art and may	indications include
				be used or routinely modified	inflammation and
				to assess the ability of	inflammatory disorders.
				polypeptides of the invention	Preferred indications include
				(including antibodies and	blood disorders (e.g., as
				agonists or antagonists of the	described below under
·				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
				modulate the expression of	"Cardiovascular Disorders").
				multiple genes. Exemplary	Preferred indications include
				assays for transcription	autoimmune diseases (e.g.,
				through the STAT6 response	rheumatoid arthritis, systemic
				element that may be used or	lupus erythematosis, multiple
				routinely modified to test	sclerosis and/or as described
				STAT6 response element	below) and
				activity of the polypeptides of	immunodeficiencies (e.g., as
				the invention (including	described below).
				antibodies and agonists or	Preferred indications include

		antagonists of the invention)	neoplastic diseases (e.g.,
		include assays disclosed in	leukemia, lymphoma,
		Berger et al., Gene 66:1-10	melanoma, and/or as described
		(1998); Cullen and Malm,	below under
		Methods in Enzymol 216:362-	"Hyperproliferative
		368 (1992); Henthorn et al.,	Disorders"). Preferred
		Proc Natl Acad Sci USA	indications include neoplasms
		85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
		et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
		(1998); Moffatt et al.,	prostate, breast, lung, colon,
		Transplantation 69(7):1521-	pancreatic, esophageal,
		1523 (2000); Curiel et al., Eur	stomach, brain, liver and
		J Immunol 27(8):1982-1987	urinary cancer. Other preferred
		(1997); and Masuda et al., J	indications include benign
		Biol Chem 275(38):29331-	dysproliferative disorders and
		29337 (2000), the contents of	pre-neoplastic conditions, such
		each of which are herein	as, for example, hyperplasia,
_		incorporated by reference in its	metaplasia, and/or dysplasia.
		entirety. T cells that may be	Preferred indications include
		used according to these assays	anemia, pancytopenia,
		are publicly available (e.g.,	leukopenia, thrombocytopenia,
		through the ATCC).	Hodgkin's disease, acute
		Exemplary T cells that may be	lymphocytic anemia (ALL),
		used according to these assays	plasmacytomas, multiple
		include the SUPT cell line,	myeloma, Burkitt's lymphoma,
		which is a suspension culture	arthritis, AIDS, granulomatous
		of IL-2 and IL-4 responsive T	disease, inflammatory bowel
		cells.	disease, sepsis, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted

					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious
486	HSDAJ46	1434	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as
				involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention	described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred

	(including antibodies and	indication is infection (e.g., an
	agonists or antagonists of the	infectious disease as described
	invention) include assays	below under "Infectious
	disclosed in Berger et al., Gene	Disease"). Preferred
	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988);	"Hyperproliferative
	Aramburu et al., J Exp Med	Disorders"). Preferred
	182(3):801-810 (1995); De	indications include neoplasms
	Boer et al., Int J Biochem Cell	and cancers, such as, for
	Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
	Fraser et al., Eur J Immunol	and prostate, breast, lung,
-	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. NK	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,
	according to these assays are	metaplasia, and/or dysplasia.
	publicly available (e.g.,	Preferred indications also
	through the ATCC).	include anemia, pancytopenia,
	Exemplary human NK cells	leukopenia, thrombocytopenia,
	that may be used according to	Hodgkin's disease, acute
	these assays include the NK-	lymphocytic anemia (ALL),
	YT cell line, which is a human	plasmacytomas, multiple
	natural killer cell line with	myeloma, Burkitt's lymphoma,
	cytolytic and cytotoxic	arthritis, AIDS, granulomatous
	activity.	disease, inflammatory bowel

					disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
487	HSDEK49	1435	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple
				antagonists of the invention) include assays disclosed in	Crohn's disease, multiple sclerosis and/or as described

		Beroer et al Gene 66·1-10	helow) immunodeficiencies
		(1998): Cullen and Malm.	(e.g., as described below).
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
		cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
		through the ATCC).	include neoplastic diseases
		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		may be used according to these	and/or as described below
		assays include the CTLL cell	under "Hyperproliferative
		line, which is an IL-2	Disorders"). Additionally,
		dependent suspension culture	highly preferred indications
		of T cells with cytotoxic	include neoplasms and
		activity.	cancers, such as, for example,
	-		Ieukemia, Iymphoma,
			melanoma, glioma (e.g.,
			malignant glioma), solid
-			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative

					disorders and are neonlastic
					conditions and be for
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
-					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
_					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HSDEK49	1435	Regulation of	Assays for the regulation of	A highly preferred
487			transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
			adipocytes	may be used or routinely	indication is a complication

	modified to assess the ability	associated with diabetes (e.g.,
	of polypeptides of the	diabetic retinopathy, diabetic
	invention (including antibodies	nephropathy, kidney disease
	and agonists or antagonists of	(e.g., renal failure,
	the invention) to regulate	nephropathy and/or other
	transcription of Malic Enzyme,	diseases and disorders as
	a key enzyme in lipogenesis.	described in the "Renal
	Malic enzyme is involved in	Disorders" section below),
	lipogenesisand its expression is	diabetic neuropathy, nerve
	stimulted by insulin. ME	disease and nerve damage
	promoter contains two direct	(e.g., due to diabetic
	repeat (DR1)- like elements	neuropathy), blood vessel
	MEp and MEd identified as	blockage, heart disease, stroke,
	putative PPAR response	impotence (e.g., due to diabetic
	elements. ME promoter may	neuropathy or blood vessel
	also responds to AP1 and other	blockage), seizures, mental
	transcription factors.	confusion, drowsiness,
	Exemplary assays that may be	nonketotic hyperglycemic-
	used or routinely modified to	hyperosmolar coma,
	test for regulation of	cardiovascular disease (e.g.,
	transcription of Malic Enzyme	heart disease, atherosclerosis,
_	(in adipoocytes) by	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment

				(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
				Biol Chem, 274(25):17997-	blindness), ulcers and impaired
				8004 (1999); Ijpenberg, A., et	wound healing, and infection
				al., J Biol Chem,	(e.g., infectious diseases and
				272(32):20108-20117 (1997);	disorders as described in the
				Berger, et al., Gene 66:1-10	"Infectious Diseases" section
				(1988); and, Cullen, B., et al.,	below, especially of the
				Methods in Enzymol.	urinary tract and skin), carpal
				216:362–368 (1992), the	tunnel syndrome and
				contents of each of which is	Dupuytren's contracture).
				herein incorporated by	An additional highly preferred
				reference in its entirety.	indication is obesity and/or
				Hepatocytes that may be used	complications associated with
				according to these assays are	obesity. Additional highly
				publicly available (e.g.,	preferred indications include
				through the ATCC) and/or	weight loss or alternatively,
				may be routinely generated.	weight gain. Aditional
				Exemplary hepatocytes that	highly preferred indications are
				may be used according to these	complications associated with
				assays includes the H4IIE rat	insulin resistance.
				liver hepatoma cell line.	
487	HSDEK49	1435	MIP-1a in HMC		
	HSDER95	1436	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
488				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,

Deregulated expression of IL-6   reducing) IL-6 production. A	reducing) IL-6 production. A
has been linked to autoimmune	highly preferrred indication is
disease, plasmacytomas,	the stimulation or enhancement
myelomas, and chronic	of mucosal immunity. Highly
hyperproliferative diseases.	preferred indications include
Assays for immunomodulatory	blood disorders (e.g., as
and differentiation factor	described below under
 proteins produced by a large	"Immune Activity", "Blood-
variety of cells where the	Related Disorders", and/or
expression level is strongly	"Cardiovascular Disorders"),
regulated by cytokines, growth	and infection (e.g., as
 factors, and hormones are well	described below under
 known in the art and may be	"Infectious Disease"). Highly
used or routinely modified to	preferred indications include
 assess the ability of	autoimmune diseases (e.g.,
 polypeptides of the invention	rheumatoid arthritis, systemic
(including antibodies and	lupus erythematosis, multiple
agonists or antagonists of the	sclerosis and/or as described
invention) to mediate	below) and
immunomodulation and	immunodeficiencies (e.g., as
differentiation and modulate T	described below). Highly
 cell proliferation and function.	preferred indications also
Exemplary assays that test for	include boosting a B cell-
immunomodulatory proteins	mediated immune response
evaluate the production of	and alternatively suppressing a
cytokines, such as IL-6, and	B cell-mediated immune
the stimulation and	response. Highly preferred
upregulation of T cell	indications include
proliferation and functional	inflammation and
 activities. Such assays that	inflammatory
may be used or routinely	disorders. Additional highly

	modified to tout	obulous andionipus boundons
	inounted to lest	preferred mulcamons include
 	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
 	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
 	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
 	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	when activated by antigen	leukopenia, thrombocytopenia,
	and/or cytokines, initiate and	Hodgkin's disease, acute
	upregulate T cell proliferation	lymphocytic anemia (ALL),
 	and functional activities.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
		granulomatous disease,

inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	Kinase assay: measures the phosphorylation of Elk-1, an indication of activation of extracellular signal regulated kinase (ERK). ERK pathway regulates cell growth, proliferation and differentiation. Cells were pretreated with SID supernatants for 15-18 hours, and then 100 nM of insulin was added to stimulate ERK kinase. Phosphorylation of Elk-1 was measured after a 20 minute incubation. Preadplocytes that may be used according to these assays are
	Inhibition of adipocyte ERK signaling pathway.
	1437
	HSDEZ20
	489

htrough the ATCC) and may be routinely general Exemplary mouse adipocally and the ATCC) and may be routinely general early and the assay include 313-L1 cells. 3 is an adherent mouse preadipocyte cell line the continuous substrain of fibroblast cells develope through clonal isolation undergo a pre-adipocyte adipose-like conversion appropriate differentiatic conditions known in the Cells were differentiated adipose-like state before used in the screen. See et al., Cell 3: 127-133 (I the contents of which at herein incorporated by reference in its entirety.  HSDEZ20 I437 Activation of JNK Kinase assay. JNK kinas sasays for signal transd, in immune cells set in immune cells activation, or apoptosis eosinophils).  be used or routinely mo to assess the ability of to assess the ability of	and/or nerated. dipocyte ed ssays s. 3T3-L1 e te that is a n of 3T3 loped tion and cyte to sion under tiation the art. iated to an sfore being See Green state state h are by	kinase Highly preferred indications include asthma, allergy, bliferation, hypersensitivity reactions, inflammation, and inflammatory disorders.  Additional highly preferred indications include immune
1437	publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. Cells were differentiated to an adipose-like state before being used in the screen. See Green et al., Cell 3: 127-133 (1974), the contents of which are herein incorporated by reference in its entirety.	
HSDEZ20		
		HSDEZ20

	(including antibodies and	(e g as described below under
	agonists or antagonists of the	"Immine Activity" and
-	invention) to promote or	"Blood-Related Disorders"),
 	inhibit cell proliferation,	autoimmune diseases (e.g.,
 	activation, and apoptosis.	rheumatoid arthritis, systemic
	Exemplary assays for JNK	lupus erythematosis, Crohn"s
	kinase activity that may be	disease, multiple sclerosis
 	used or routinely modified to	and/or as described below),
	test JNK kinase-induced	immunodeficiencies (e.g., as
 	activity of polypeptides of the	described below). Highly
	invention (including antibodies	preferred indications also
	and agonists or antagonists of	include boosting or inhibiting
	the invention) include the	immune cell proliferation.
 	assays disclosed in Forrer et	Preferred indications include
	al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
	1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
	Cell Res 247(2): 495-504	described below under
	(1999); Kyriakis JM, Biochem	"Hyperproliferative
	Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
	Chang and Karin, Nature	indications include boosting an
	410(6824):37-40 (2001); and	eosinophil-mediated immune
	Cobb MH, Prog Biophys Mol	response, and suppressing an
	Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
	the contents of each of which	response.
	are herein incorporated by	
	reference in its entirety.	
	Exemplary cells that may be	
	used according to these assays	
	include eosinophils.	
	Eosinophils are important in	
	the late stage of allergic	

reactions; they are recruited to tissues and mediate the inflammatory response of late stage altergic reaction.  Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention including antibodies and agonists or antagonists of the invention in modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" (Clin Exp Immunol: Oct, 122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signalling by nitric oxide in eosinophils" J Exp Med; Feb 2:187(3):415-25 (1998); J Allergy Clin Immunol 1999																				-											
	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt1):565-74; and,

			Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep; 104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	
HSDFW45	1438	SEAP in 293/ISRE		
HSDFW45	1438	Activation of transcription through cAMP response element (CRE) in preadipocytes.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other

3T3-L1/CRE reporter assav	diseases and disorders as
may be used to identify factors	described in the "Renal
that activate the cAMP	Disorders" section below),
signaling pathway. CREB	diabetic neuropathy, nerve
plays a major role in	disease and nerve damage
adipogenesis, and is involved	(e.g., due to diabetic
in differentiation into	neuropathy), blood vessel
adipocytes. CRE contains the	blockage, heart disease, stroke,
binding sequence for the	impotence (e.g., due to diabetic
transcription factor CREB	neuropathy or blood vessel
(CRE binding protein).	blockage), seizures, mental
Exemplary assays for	confusion, drowsiness,
transcription through the	nonketotic hyperglycemic-
cAMP response element that	hyperosmolar coma,
may be used or routinely	cardiovascular disease (e.g.,
modified to test cAMP-	heart disease, atherosclerosis,
response element activity of	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in Berger et al., Gene	section below), dyslipidemia,
66:1-10 (1998); Cullen and	endocrine disorders (as
Malm, Methods in Enzymol	described in the "Endocrine
216:362-368 (1992); Henthorn	Disorders" section below),
et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
et al., Mol Cell Biol	blindness), ulcers and impaired
20(3):1008-1020 (2000); and	wound healing, and infection
Klemm et al., J Biol Chem	(e.g., infectious diseases and
273:917-923 (1998), the	disorders as described in the

				herein incorporated by	below, especially of the
_				reference in its entirety. Pre-	urinary tract and skin), carpal
				adipocytes that may be used	tunnel syndrome and
	-			according to these assays are	Dupuytren's contracture).
	_			publicly available (e.g.,	Additional highly preferred
				through the ATCC) and/or	indications are complications
-				may be routinely generated.	associated with insulin
				Exemplary mouse adipocyte	resistance.
				cells that may be used	
				according to these assays	
•				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
HS HS	HSDFW45	1438	SEAP in HIB/CRE		
	HSDFW45	1438	Activation of	This reporter assay measures	Highly preferred indications
490			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and

	activation of transcription	inflammatory disorders.
	through the GATA3 response	Preferred indications also
	element are well-known in the	include blood disorders (e.g.,
	art and may be used or	as described below under
	routinely modified to assess	"Immune Activity", "Blood-
	 the ability of polypeptides of	Related Disorders", and/or
	the invention (including	"Cardiovascular Disorders").
	antibodies and agonists or	Preferred indications include
	antagonists of the invention) to	autoimmune diseases (e.g.,
	regulate GATA3 transcription	rheumatoid arthritis, systemic
	factors and modulate	lupus erythematosis, multiple
	expression of mast cell genes	sclerosis and/or as described
	important for immune response	below) and
	development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
_	element that may be used or	diseases (e.g., leukemia,
	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	stomach, brain, liver, and
•	and agonists or antagonists of	urinary tract cancers and/or as
	the invention) include assays	described below under
-	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred
	Malm, Methods in Enzymol	indications include benign
	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
_	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Quant Biol 64:563-571 (1999);	Preferred indications include

i, and Biol he are last last line heral st st st					Rodriguez-Palmero et al Fur	anemia nancytonenia
(1999); Zheng and Flavell, Cell 80(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC- 1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in imman mast cells ine. human mast cell line. cytokine and chemokine					I Imminol 29/12):3014-3024	lenkonenia thrombooxtonenia
(1975). Liching and Travell,  (1976). Later and Travell,  Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell line stablished from the peripheral blood of a patient with mast cell line activation of the NFAT in mast cell increases.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT in mast cells in mmanure cells (such as been linked to cytokine and chemokine).					7 minimiot 27(12):37 14-3724 (1000): Zhang and Elevioll	leunopenia, unomoces repenia,
Cell 89(4)::87-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in human mast cell line. immune cells (such activation of NFAT in mast as mast cells). Cylokine and chemokine					(1999), Lifelig allu Flavell,	leureillias, flougrill s disease,
Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell lenkemia, and exhibits many characteristics of immature mast cells.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in human mast cell line. immune cells (such Activation of NFAT in mast as mast cells).					Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.    HSDFW45					Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell line established from the peripheral blood of a patient with mast cell line many characteristics of immature mast cells.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in human mast cell line.  Activation of NFAT in mast cells (such as mast cells).					14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
HSDFW45  HSPFW45  HSDFW45  HSDFW45  HSDFW5  HSDFW7  HSDFW7  HSDFW7  HSDFW7  HWAT  HSDFW7  HWAT  HWAN  HWAT  HOWAN  HWAT  HANDRH SHAT  HANDRH					contents of each of which are	lymphoma, arthritis, AIDS,
reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in human mast cell line. immune cells (such as been linked to cytokine and chemokine					herein incorporated by	granulomatous disease,
cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-I cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-I response element in immune cells (such man mast cell line. immune cells (such as been linked to cytokine and chemokine					reference in its entirety. Mast	inflammatory bowel disease,
according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in human mast cell line. immune cells (such activation of NFAT in mast as mast cells).					cells that may be used	sepsis, neutropenia,
hrough the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-  I cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in immune cells (such as been linked to cytokine and chemokine cells).					according to these assays are	neutrophilia, psoriasis,
HSDFW45 1438 Activation of This reporter assay measures transcription as mast cell line. which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in human mast cell line. immune cells (such Activation of NFAT in mast as mast cells).	_				publicly available (e.g.,	suppression of immune
Exemplary human mast cells that may be used according to these assays include the HMC-  1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.  HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in immune cells (such as mast cells).  cytokine and chemokine					through the ATCC).	reactions to transplanted
HSDFW45 1438 Activation of immature mast cells.  HSDFW45 1438 Activation of immature mast cells. Thus reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in immune cells (such as mast cells).  cytokine and chemokine					Exemplary human mast cells	organs and tissues, hemophilia,
HSDFW45 1438 Activation of through NFAT signaling pathway in HMC-1 response element in imman mast cell line.  HSDFW45 (such as mast cells).  HSDFW45 (such as mast cells).					that may be used according to	hypercoagulation, diabetes
HSDFW45 1438 Activation of This reporter assay measures transcription through NFAT signaling pathway in HMC-1 response element in immune cells (such as mast cells).					these assays include the HMC-	mellitus, endocarditis,
HSDFW45 1438 Activation of This reporter assay measures transcription ast cells human mast cell line. Immune cells (such immune cells (such as mast cells).					1 cell line, which is an	meningitis, and Lyme Disease.
HSDFW45 1438 Activation of through NFAT signaling pathway in HMC-1 response element in immune cells (such as mast cells).					immature human mast cell line	
HSDFW45 1438 Activation of transcription through NFAT signaling pathway in HMC-1 response element in immune cells (such as mast cells).					established from the peripheral	
HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT signaling pathway in HMC-1 response element in human mast cell line. immune cells (such as mast cells).					blood of a patient with mast	
HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in human mast cell line. immune cells (such as mast cells).					cell leukemia, and exhibits	
HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in human mast cell line. immune cells (such as mast cells).					many characteristics of	
HSDFW45 1438 Activation of This reporter assay measures transcription activation of the NFAT through NFAT signaling pathway in HMC-1 response element in human mast cell line. immune cells (such as mast cells).					immature mast cells.	
transcription activation of the NFAT signaling pathway in HMC-1 response element in immune cells (such as mast cells).		HSDFW45	1438	Activation of	This reporter assay measures	Highly preferred indications
signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine	490			transcription	activation of the NFAT	include allergy, asthma, and
human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine				through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
Activation of NFAT in mast cells has been linked to cytokine and chemokine				response element in	human mast cell line.	indications include infection
cells has been linked to cytokine and chemokine				immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
				as mast cells).	cells has been linked to	described below under
					cytokine and chemokine	"Infectious Disease"), and
					production. Assays for the	inflammation and

	activation of transcription	inflammatory disorders.
	through the Nuclear Factor of	Preferred indications also
	 Activated T cells (NFAT)	include blood disorders (e.g.,
	 response element are well-	as described below under
	known in the art and may be	"Immune Activity", "Blood-
	used or routinely modified to	Related Disorders", and/or
	assess the ability of	"Cardiovascular Disorders").
	polypeptides of the invention	Preferred indications include
	(including antibodies and	autoimmune diseases (e.g.,
	agonists or antagonists of the	rheumatoid arthritis, systemic
	invention) to regulate NFAT	lupus erythematosis, multiple
	transcription factors and	sclerosis and/or as described
	 modulate expression of genes	below) and
	 involved in	immunodeficiencies (e.g., as
	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	 (including antibodies and	described below under
•	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	 66:1-10 (1998); Cullen and	dysproliferative disorders and
	 Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include

		31(10):1221-1236 (1999); Ali et al J Immunol	leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia
		et al J Immunol	leukemias, Hodgkin's disease, acute lymphocytic anemia
			acute lymphocytic anemia
		165(12):7215-7223 (2000);	
		Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
		16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
		al., J Exp Med 188:527-537	granulomatous disease,
		(1998), the contents of each of	inflammatory bowel disease,
		which are herein incorporated	sepsis, neutropenia,
		by reference in its entirety.	neutrophilia, psoriasis,
		Mast cells that may be used	suppression of immune
		according to these assays are	reactions to transplanted
		publicly available (e.g.,	organs and tissues, hemophilia,
		through the ATCC).	hypercoagulation, diabetes
		Exemplary human mast cells	mellitus, endocarditis,
		that may be used according to	meningitis, and Lyme Disease.
		these assays include the HMC-	
		1 cell line, which is an	
		immature human mast cell line	
		established from the peripheral	
		blood of a patient with mast	
		cell leukemia, and exhibits	
		many characteristics of immature mast cells.	
HSDFW45 1438 SEAP in	SEAP in Jurkat/IL4		
490 promote	promoter		
HSDFW45 1438	SEAP in Jurkat/IL4		
490 promote co-stim	promoter (antiCD3 co-stim)		
HSDJA15 1439 Activati	Activation of	Kinase assay. Kinase assays,	A highly preferred

491	Adinocyte PI3	for example an GSK-3 assays	embodiment of the invention
	Kinase Signalling	for D13 kinase signal	includes a method for
	Niliase Signannig	101 1 13 Miliase Signal	
	Pathway	transduction that regulate	increasing adipocyte survival
		glucose metabolism and cell	An alternative highly preferred
		survival are well-known in the	embodiment of the invention
		art and may be used or	includes a method for
		routinely modified to assess	decreasing adipocyte survival.
		the ability of polypeptides of	A preferred embodiment of the
		the invention (including	invention includes a method
		antibodies and agonists or	for stimulating adipocyte
		antagonists of the invention) to	proliferation. An alternative
		promote or inhibit glucose	highly preferred embodiment
		metabolism and cell survival.	of the invention includes a
		Exemplary assays for PI3	method for inhibiting
		kinase activity that may be	adipocyte proliferation. A
20		used or routinely modified to	preferred embodiment of the
		test PI3 kinase-induced activity	invention includes a method
		of polypeptides of the	for stimulating adipocyte
		invention (including antibodies	differentiation. An alternative
		and agonists or antagonists of	highly preferred embodiment
		the invention) include assays	of the invention includes a
		disclosed in Forrer et al., Biol	method for inhibiting
		Chem 379(8-9):1101-1110	adipocyte differentiation.
		(1998); Nikoulina et al.,	Highly preferred indications
		Diabetes 49(2):263-271	include endocrine disorders
		(2000); and Schreyer et al.,	(e.g., as described below under
-		Diabetes 48(8):1662-1666	"Endocrine Disorders").
		(1999), the contents of each of	Preferred indications include
		which are herein incorporated	neoplastic diseases (e.g.,
		by reference in its entirety.	lipomas, liposarcomas, and/or
		Mouse adipocyte cells that	as described below under

	may be used according to these	"Hyperproliferative
	assays are publicly available	Disorders"), blood disorders
	(e.g., through the ATCC).	(e.g., hypertension, congestive
	Exemplary mouse adipocyte	heart failure, blood vessel
	cells that may be used	blockage, heart disease, stroke,
	according to these assays	impotence and/or as described
	include 3T3-L1 cells. 3T3-L1	below under "Immune
	is an adherent mouse	Activity", "Cardiovascular
	preadipocyte cell line that is a	Disorders", and/or "Blood-
	continous substrain of 3T3	Related Disorders"), immune
	fibroblast cells developed	disorders (e.g., as described
	through clonal isolation and	below under "Immune
	undergo a pre-adipocyte to	Activity"), neural disorders
	adipose-like conversion under	(e.g., as described below under
	appropriate differentiation	"Neural Activity and
	conditions known in the art.	Neurological Diseases"), and
		infection (e.g., as described
		ır "In
		Disease"). A highly
		preferred indication is diabetes
		mellitus. An additional
,		highly preferred indication is a
		complication associated with
		diabetes (e.g., diabetic
		retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure,
		nephropathy and/or other
		diseases and disorders as
		described in the "Renal
		Disorders" section below),

	disease and nerve damage (e.g., due to diabetic neuropathy),
	due to diabetic neuropathy),
	blood vessel blockage, heart
	disease, stroke, impotence
	(e.g., due to diabetic
	neuropathy or blood vessel
	blockage), seizures, mental
	confusion, drowsiness,
	nonketotic hyperglycemic-
	hyperosmolar coma,
	cardiovascular disease (e.g.,
	heart disease, atherosclerosis,
	microvascular disease,
	hypertension, stroke, and other
	diseases and disorders as
	described in the
	"Cardiovascular Disorders"
	section below), dyslipidemia,
	endocrine disorders (as
	described in the "Endocrine
	Disorders" section below),
	neuropathy, vision impairment
1. v	(e.g., diabetic retinopathy and
A .I. O	blindness), ulcers and impaired
	wound healing, infection (e.g.,
	infectious diseases and
	disorders as described in the
	"Infectious Diseases" section
	below, especially of the
3	urinary tract and skin), carpal

-		tunnel syndrome and
		Dupuytren's contracture).
		An additional highly preferred
		indication is obesity and/or
	-	complications associated with
		obesity. Additional highly
		preferred indications include
		weight loss or alternatively,
		weight gain. Additional
		highly preferred indications are
		complications associated with
		insulin resistance.
		Additional highly preferred
	-	indications are disorders of the
		musculoskeletal systems
		 including myopathies,
		 muscular dystrophy, and/or as
		described herein.
		Additional highly preferred
		 indications include,
		 hypertension, coronary artery
		disease, dyslipidemia,
		gallstones, osteoarthritis,
		degenerative arthritis, eating
		disorders, fibrosis, cachexia,
		and kidney diseases or
		 disorders. Highly preferred
		indications include neoplasms
		and cancer, such as, lipoma,
		liposarcoma, lymphoma,
		I and a family and business that

					and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
491	HSDJA15	1439	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,

		ped	ies		p		ated	ional	us		pu			ghly	sis.	suc	S	a,			,,	us		ıple,				ıst,		in,	
	, multiple	as descril	deficienc	d below)	l-mediate	e, and	cell-med	e. Addi	indicatio	ation and	sorders, a	nage in	umatoid	litional h	ion is set	I indication	ic disease	lymphom	ed below	diferative	ditionally	indicatio	ns and	, for exan	ioma,	na (e.g.,	a), solid	state, brea	creatic,	nach, bra	
	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	mmune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	
	Crohn"	scleros	below).	(e.g., a	boostin	immun	suppres	immun	highly	include	inflam	treating	patients	arthritis	preferre	Highly	include	(e.g., le	and/or	" nnder	Disorde	highly	include	cancers	leukem	melano	malign	tumors	lung, co	esopha	
	ntion)	ni be	1-10	ılm,	16:362-	et al.,	šA	and	ıes	the	ch are		γ. T		ys are	:		ells that	g to these	Tr cell		culture	ic								
	f the inve	s disclose	Gene 66:	n and Ma	nzymol 2	lenthorn	ad Sci US	5 (1988);	Virus Ger	7 (1997),	ch of whi	orated by	ts entirety	be used	these assa	lable (e.g.	TCC).	ouse T ce	according	e the CTI	an IL-2	spension	h cytotox								
	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety.	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.							
-	anta	inch	Berg	(199	Met	368	Proc	85:6	Blac	12(2	cont	here	refer	cells	acco	Iqnd	thro	Exel	may	assa	line,	debe	of T	activ					-		_
<u> </u>													-																		
																										· · ·					

					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
				-	conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
=		_			Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
20					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
			_		hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
* * .					under "Infectious Disease").
491	HSDJA15	1439	Activation of transcription	This reporter assay measures activation of the GATA-3	Highly preferred indications include allergy, asthma, and

through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
response element in	human mast cell line.	indications include infection
immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
as mast cells).	cells has been linked to	described below under
	cytokine and chemokine	"Infectious Disease"), and
	production. Assays for the	inflammation and
	activation of transcription	inflammatory disorders.
	through the GATA3 response	Preferred indications also
	element are well-known in the	include blood disorders (e.g.,
	art and may be used or	as described below under
	routinely modified to assess	"Immune Activity", "Blood-
	the ability of polypeptides of	Related Disorders", and/or
	the invention (including	"Cardiovascular Disorders").
	antibodies and agonists or	Preferred indications include
	antagonists of the invention) to	autoimmune diseases (e.g.,
	regulate GATA3 transcription	rheumatoid arthritis, systemic
	factors and modulate	lupus erythematosis, multiple
	expression of mast cell genes	sclerosis and/or as described
	important for immune response	below) and
	development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
	element that may be used or	diseases (e.g., leukemia,
	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred

				Malm Methods in Enzymol	indications include benian
				Maini, inculous in Linzymoi	
	_			216:362-368 (1992); Henthorn	dysproliterative disorders and
				et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
				85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
				Quant Biol 64:563-571 (1999);	Preferred indications include
				Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
				J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HSDJA15	1439	Production of IL-5	IL-5 FMAT. Assays for	A highly preferred
491				immunomodulatory proteins	embodiment of the invention

	secreted by TH2 cells, mast	includes a method for
	cells, basophils, and	inhibiting (e.g., reducing) IL-5
	eosinophils that stimulate	production. An alternative
	eosinophil function and B cell	highly preferred embodiment
	Ig production and promote	of the invention includes a
	polarization of CD4+ cells into	method for stimulating (e.g.,
	TH2 cells are well known in	increasing) IL-5 production.
	the art and may be used or	A highly preferred
	routinely modified to assess	embodiment of the invention
	the ability of polypeptides of	includes a method for
	the invention (including	stimulating (e.g., increasing)
	antibodies and agonists or	immunoglobulin production.
	antagonists of the invention) to	An alternative highly preferred
	mediate immunomodulation,	embodiment of the invention
	stimulate immune cell	includes a method for
	function, modulate B cell Ig	inhibiting (e.g., decreasing)
	production, modulate immune	immunoglobulin production.
	cell polarization, and/or	A highly preferred indication
	mediate humoral or cell-	includes allergy. A highly
	mediated immunity.	preferred indication includes
	Exemplary assays that test for	asthma. A highly preferred
	immunomodulatory proteins	indication includes rhinitis.
	evaluate the production of	An additional highly preferred
	cytokines, such as IL-5, and	indication is infection (e.g., an
	the stimulation of eosinophil	infectious disease as described
	function and B cell Ig	below under "Infectious
	production. Such assays that	Disease"), and inflammation
-	may be used or routinely	and inflammatory disorders.
	modified to test	Preferred indications include
	immunomodulatory activity of	blood disorders (e.g., as
	polypeptides of the invention	described below under

(inclu	(including antibodies and	"Immune Activity", "Blood-
agoni	agonists or antagonists of the	Related Disorders", and/or
invent	invention) include the assays	"Cardiovascular Disorders").
 disclo	disclosed in Miraglia et al., J	Preferred indications include
Biome	Biomolecular Screening 4:193-	autoimmune diseases (e.g.,
204 (1	204 (1999); Rowland et al.,	rheumatoid arthritis, systemic
"Lym	"Lymphocytes: a practical	lupus erythematosis, multiple
 appro	approach" Chapter 6:138-160	sclerosis and/or as described
(2000	(2000); Ohshima et al., Blood	below) and
 (92(9):	92(9):3338-3345 (1998); Jung	immunodeficiencies (e.g., as
 et al.,	et al., Eur J Immunol	described below). Preferred
25(8):	25(8):2413-2416 (1995); Mori	indications include neoplastic
 et al.,	et al., J Allergy Clin Immunol	diseases (e.g., leukemia,
106(1	106(1 Pt 2):558-564 (2000);	lymphoma, melanoma, and/or
and K	oning et al., Cytokine	as described below under
9(6):4	9(6):427-436 (1997), the	"Hyperproliferative
 conter	contents of each of which are	Disorders"). Preferred
 herein	herein incorporated by	indications include neoplasms
refere	reference in its entirety.	and cancers, such as, leukemia,
 Huma	Human T cells that may be	lymphoma, melanoma, and
 pesn nsed s	used according to these assays	prostate, breast, lung, colon,
may b	may be isolated using	pancreatic, esophageal,
techni	techniques disclosed herein or	stomach, brain, liver and
other	otherwise known in the art.	urinary cancer. Other preferred
Huma	Human T cells are primary	indications include benign
 huma	human lymphocytes that	dysproliferative disorders and
 matur	mature in the thymus and	pre-neoplastic conditions, such
expre	express a T cell receptor and	as, for example, hyperplasia,
CD3,	CD3, CD4, or CD8. These	metaplasia, and/or dysplasia.
cells r	cells mediate humoral or cell-	Preferred indications include
media	mediated immunity and may	anemia, pancytopenia,

	nolvnentides of the invention	method for inhibiting
 -	(including antibodies and	endothelial cell proliferation.
	agonists or antagonists of the	A highly preferred
	invention) include the assays	embodiment of the invention
	disclosed in Romeo et al.,	includes a method for
	Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
	(2000); Messmer et al., Br J	growth. An alternative highly
	Pharmacol 127(7): 1633-1640	preferred embodiment of the
	(1999); and J Atheroscler	invention includes a method
 	Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
	the contents of each of which	growth. A highly preferred
 _	are herein incorporated by	embodiment of the invention
-	reference in its entirety.	includes a method for
 	Endothelial cells that may be	stimulating apoptosis of
	used according to these assays	endothelial cells. An
	are publicly available (e.g.,	alternative highly preferred
	through commercial sources).	embodiment of the invention
	Exemplary endothelial cells	includes a method for
	that may be used according to	inhibiting (e.g., decreasing)
	these assays include bovine	apoptosis of endothelial cells.
	aortic endothelial cells	A highly preferred
	(bAEC), which are an example	embodiment of the invention
	of endothelial cells which line	includes a method for
	blood vessels and are involved	stimulating angiogenisis. An
	in functions that include, but	alternative highly preferred
	are not limited to,	embodiment of the invention
	angiogenesis, vascular	includes a method for
-	permeability, vascular tone,	inhibiting angiogenesis. A
	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for reducing cardiac

hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include
neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system
(e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis
and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic
hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular,
disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as

stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and	as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis,	hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as	thrombophlebitis, lymphangitis, and lymphadema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions),	implant fixation, scarring,

	ischemia reperfusion injury,
	rheumatoid arthritis,
	cerebrovascular disease, renal
	diseases such as acute renal
<u> </u>	failure, and osteoporosis.
	Additional highly preferred
	indications include stroke,
3	graft rejection, diabetic or
	other retinopathies, thrombotic
	and coagulative disorders,
	vascularitis, lymph
	angiogenesis, sexual disorders,
	age-related macular
	degeneration, and treatment
	/prevention of endometriosis
	and related conditions.
	Additional highly preferred
	indications include fibromas,
	heart disease, cardiac arrest,
1	heart valve disease, and
	vascular disease. Preferred
	indications include blood
3	disorders (e.g., as described
	below under "Immune
	Activity", "Blood-Related
	Disorders", and/or
	"Cardiovascular Disorders").
I	Preferred indications include
	autoimmune diseases (e.g.,
H	rheumatoid arthritis, systemic
	lupus erythematosis, multiple

sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.		Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders.  Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood- as described below under "Cardiovascular Disorders").  Preferred indications include autoimmune diseases (e.g.,
		This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
	IL-6 in HUVEC	Activation of transcription through NFAT response element in immune cells (such as mast cells).
	1440	1441
	HSDJJ82	HSDJL42
	492	493

	ago	agonists or antagonists of the	rheumatoid arthritis, systemic
	inve	invention) to regulate NFAT	lupus erythematosis, multiple
	tran	transcription factors and	sclerosis and/or as described
	om	modulate expression of genes	below) and
	invo	involved in	immunodeficiencies (e.g., as
	nmi	immunomodulatory functions.	described below). Preferred
	Exe	Exemplary assays for	indications include neoplastic
	tran	transcription through the	diseases (e.g., leukemia,
	NF/	NFAT response element that	lymphoma, melanoma,
	may	may be used or routinely	prostate, breast, lung, colon,
	oom moo	modified to test NFAT-	pancreatic, esophageal,
	resp	response element activity of	stomach, brain, liver, and
-	(lod	polypeptides of the invention	urinary tract cancers and/or as
	(inc	(including antibodies and	described below under
	ago	agonists or antagonists of the	"Hyperproliferative
	inve	invention) include assays	Disorders"). Other preferred
	disc	disclosed in Berger et al., Gene	indications include benign
		66:1-10 (1998); Cullen and	dysproliferative disorders and
	Mal	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et a	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6	85:6342-6346 (1988); De Boer	Preferred indications include
	et a	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et a	et al., J Immunol	leukemias, Hodgkin's disease,
	165	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hut	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	163	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al.,	al., J Exp Med 188:527-537	granulomatous disease,
	(196	(1998), the contents of each of	inflammatory bowel disease,

			which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
HSDJL42	1441	ICAM in 0E19		
HSDJM31	1442	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation,	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An adipocyte differentiation. An

	activation, and differentiation.	alternative highly preferred
	 Exemplary assays for ERK	embodiment of the invention
	kinase activity that may be	includes a method for
	used or routinely modified to	inhibiting adipocyte
	test ERK kinase-induced	differentiation. A highly
	activity of polypeptides of the	preferred embodiment of the
	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
	the invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
	   al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	   1110 (1998); Le Marchand-	of the invention includes a
	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	 107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
	   410(6824):37-40 (2001); and	"Endocrine Disorders").
	 Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the contents of each of which	diseases (e.g., lipomas,
	 are herein incorporated by	liposarcomas, and/or as
	 reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
	according to these assays	stroke, impotence and/or as

a	fibroblast cells developed bisorders"), immune disorders through clonal isolation and undergo a pre-adipocyte to "Immune Activity"), neural	der	"Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication.	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as	described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage heart disease stroke

neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,

weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred	indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include	hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms	and cancer, such as, Iymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred

					indications include benign
					dysproliferative disorders and
					pre-free plastic conditions, such
					as, 10r example, nyperplasia, metaplasia, and/or dysplasia.
494	HSDJM31	1442	VEGF in SW480		
495	HSDSB09	1443	SEAP in 293/ISRE		
	HSDSB09	1443	Regulation of	Assays for the regulation of	A highly preferred indication
495			transcription via	transcription through the	is diabetes mellitus.
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic
				polypeptides of the invention	retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to activate the	nephropathy and/or other
				DMEF1 response element in a	diseases and disorders as
				reporter construct (such as that	described in the "Renal
				containing the GLUT4	Disorders" section below),
				promoter) and to regulate	diabetic neuropathy, nerve
				insulin production. The	disease and nerve damage
				DMEF1 response element is	(e.g., due to diabetic
				present in the GLUT4	neuropathy), blood vessel
				promoter and binds to MEF2	blockage, heart disease, stroke,
				transcription factor and another	impotence (e.g., due to diabetic
				transcription factor that is	neuropathy or blood vessel
				required for insulin regulation	blockage), seizures, mental
				of Glut4 expression in skeletal	confusion, drowsiness,

	muscle. GLUT4 is the primary	nonketotic hyperglycemic-
		hyperosmolar coma,
	transporter in fat and muscle	cardiovascular disease (e.g.,
	tissue. Exemplary assays that	heart disease, atherosclerosis,
	may be used or routinely	microvascular disease,
	modified to test for DMEF1	hypertension, stroke, and other
	response element activity (in	diseases and disorders as
	 adipocytes and pre-adipocytes)	described in the
	 by polypeptides of the	"Cardiovascular Disorders"
	invention (including antibodies	section below), dyslipidemia,
	and agonists or antagonists of	endocrine disorders (as
	the invention) include assays	described in the "Endocrine
	disclosed inThai, M.V., et al., J	Disorders" section below),
	Biol Chem, 273(23):14285-92	neuropathy, vision impairment
	(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
	 Chem, 275(21):16323-8	blindness), ulcers and impaired
	(2000); Liu, M.L., et al., J Biol	wound healing, and infection
	 Chem, 269(45):28514-21	(e.g., infectious diseases and
	(1994); "Identification of a 30-	disorders as described in the
	base pair regulatory element	"Infectious Diseases" section
	and novel DNA binding	below, especially of the
	protein that regulates the	urinary tract and skin). An
	human GLUT4 promoter in	additional highly preferred
	 transgenic mice", J Biol Chem.	indication is obesity and/or
_	2000 Aug 4;275(31):23666-73;	complications associated with
	Berger, et al., Gene 66:1-10	obesity. Additional highly
	(1988); and, Cullen, B., et al.,	preferred indications include
	 Methods in Enzymol.	weight loss or alternatively,
	 216:362–368 (1992), the	weight gain. Additional highly
	contents of each of which is	preferred indications are
	herein incorporated by	complications associated with

				reference in its entirety.	insulin resistance.
				Adipocytes and pre-adipocytes	
				that may be used according to	
				these assays are publicly	
				available (e.g., through the	
				ATCC) and/or may be	
				routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include the mouse 3T3-L1 cell	
				line which is an adherent	
				mouse preadipocyte cell line.	
				Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3	
				fibroblasts developed through	
				clonal isolation. These cells	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				culture conditions.	
	HSDSB09	1443	Activation of	Assays for the activation of	A highly preferred indication
495			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,

factors, and modulate	diabetic retinopathy, diabetic
expression of genes involved	nephropathy, kidney disease
in a wide variety of cell	(e.g., renal failure,
functions. For example, a	nephropathy and/or other
3T3-L1/CRE reporter assay	diseases and disorders as
may be used to identify factors	described in the "Renal
that activate the cAMP	Disorders" section below),
signaling pathway. CREB	diabetic neuropathy, nerve
plays a major role in	disease and nerve damage
adipogenesis, and is involved	(e.g., due to diabetic
in differentiation into	neuropathy), blood vessel
adipocytes. CRE contains the	blockage, heart disease, stroke,
binding sequence for the	impotence (e.g., due to diabetic
transcription factor CREB	neuropathy or blood vessel
 (CRE binding protein).	blockage), seizures, mental
Exemplary assays for	confusion, drowsiness,
transcription through the	nonketotic hyperglycemic-
cAMP response element that	hyperosmolar coma,
may be used or routinely	cardiovascular disease (e.g.,
modified to test cAMP-	heart disease, atherosclerosis,
response element activity of	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in Berger et al., Gene	section below), dyslipidemia,
66:1-10 (1998); Cullen and	endocrine disorders (as
Malm, Methods in Enzymol	described in the "Endocrine
216:362-368 (1992); Henthorn	Disorders" section below),
et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and

				et al Mol Cell Biol	blindness), ulcers and impaired
				20(3):1008-1020 (2000); and	wound healing, and infection
			-	Klemm et al., J Biol Chem	(e.g., infectious diseases and
				273:917-923 (1998), the	disorders as described in the
				contents of each of which are	"Infectious Diseases" section
	-			herein incorporated by	below, especially of the
				reference in its entirety. Pre-	urinary tract and skin), carpal
				adipocytes that may be used	tunnel syndrome and
				according to these assays are	Dupuytren's contracture).
				publicly available (e.g.,	Additional highly preferred
				through the ATCC) and/or	indications are complications
				may be routinely generated.	associated with insulin
				Exemplary mouse adipocyte	resistance.
		~		cells that may be used	
				according to these assays	
				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
	HSDSB09	1443	Activation of	Assays for the activation of	A highly preferred indication
495			transcription	transcription through the	is obesity and/or complications
			through serum	Serum Response Element	associated with obesity.
			response element in	(SRE) are well-known in the	Additional highly preferred
			pre-adipocytes.	art and may be used or	indications include weight loss
				routinely modified to assess	or alternatively, weight gain.

the ability of polypeptides of	An additional highly preferred
the invention (including	indication is diabetes mellitus.
antibodies and agonists or	An additional highly preferred
antagonists of the invention) to	indication is a complication
regulate the serum response	associated with diabetes (e.g.,
factors and modulate the	diabetic retinopathy, diabetic
expression of genes involved	nephropathy, kidney disease
 in growth. Exemplary assays	(e.g., renal failure,
for transcription through the	nephropathy and/or other
SRE that may be used or	diseases and disorders as
 routinely modified to test SRE	described in the "Renal
activity of the polypeptides of	Disorders" section below),
 the invention (including	diabetic neuropathy, nerve
antibodies and agonists or	disease and nerve damage
antagonists of the invention)	(e.g., due to diabetic
include assays disclosed in	neuropathy), blood vessel
Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
(1998); Cullen and Malm,	impotence (e.g., due to diabetic
Methods in Enzymol 216:362-	neuropathy or blood vessel
368 (1992); Henthorn et al.,	blockage), seizures, mental
Proc Natl Acad Sci USA	confusion, drowsiness,
85:6342-6346 (1988); and	nonketotic hyperglycemic-
Black et al., Virus Genes	hyperosmolar coma,
12(2):105-117 (1997), the	cardiovascular disease (e.g.,
content of each of which are	heart disease, atherosclerosis,
herein incorporated by	microvascular disease,
reference in its entirety. Pre-	hypertension, stroke, and other
adipocytes that may be used	diseases and disorders as
according to these assays are	described in the
publicly available (e.g.,	"Cardiovascular Disorders"
 through the ATCC) and/or	section below), dyslipidemia,

				may be routinely generated.	endocrine disorders (as
				Exemplary mouse adipocyte	described in the "Endocrine
				cells that may be used	Disorders" section below),
				according to these assays	neuropathy, vision impairment
				include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
				is an adherent mouse	blindness), ulcers and impaired
				preadipocyte cell line that is a	wound healing, and infection
				continuous substrain of 3T3	(e.g., infectious diseases and
				fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
				conditions known in the art.	insulin resistance.
	HSDSB09	1443	SEAP in Alk Phos		
495			C2C12		
	HSDSB09	1443	Activation of	Assays for the activation of	A preferred embodiment of
495			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or

SRE that may be used or	"Cardiovascular Disorders"),
routinely modified to test SRE	Highly preferred indications
activity of the polypeptides of	include autoimmune diseases
the invention (including	(e.g., rheumatoid arthritis,
antibodies and agonists or	systemic lupus erythematosis,
antagonists of the invention)	Crohn"s disease, multiple
include assays disclosed in	sclerosis and/or as described
Berger et al., Gene 66:1-10	below), immunodeficiencies
(1998); Cullen and Malm,	(e.g., as described below),
Methods in Enzymol 216:362-	boosting a T cell-mediated
368 (1992); Henthorn et al.,	immune response, and
Proc Natl Acad Sci USA	suppressing a T cell-mediated
85:6342-6346 (1988); and	immune response. Additional
Black et al., Virus Genes	highly preferred indications
12(2):105-117 (1997), the	include inflammation and
content of each of which are	inflammatory disorders, and
herein incorporated by	treating joint damage in
reference in its entirety. T	patients with rheumatoid
cells that may be used	arthritis. An additional highly
according to these assays are	preferred indication is sepsis.
publicly available (e.g.,	Highly preferred indications
through the ATCC).	include neoplastic diseases
Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
may be used according to these	and/or as described below
assays include the CTLL cell	under "Hyperproliferative
line, which is an IL-2	Disorders"). Additionally,
dependent suspension culture	highly preferred indications
of T cells with cytotoxic	include neoplasms and
activity.	cancers, such as, for example,
	leukemia, lymphoma,
	melanoma, glioma (e.g.,

malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication
																											_			
																	-								***					

					disease as described below under "Infectious Disease").
	HSDSB09	1443	Regulation of transcription of	Assays for the regulation of transcription of Malic Enzyme	A highly preferred indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
			adipocytes	may be used or routinely	indication is a complication
				modified to assess the ability	associated with diabetes (e.g.,
				of polypeptides of the	diabetic retinopathy, diabetic
				invention (including antibodies	nephropathy, kidney disease
				and agonists or antagonists of	(e.g., renal failure,
				the invention) to regulate	nephropathy and/or other
				transcription of Malic Enzyme,	diseases and disorders as
				a key enzyme in lipogenesis.	described in the "Renal
				Malic enzyme is involved in	Disorders" section below),
				lipogenesisand its expression is	diabetic neuropathy, nerve
				stimulted by insulin. ME	disease and nerve damage
				promoter contains two direct	(e.g., due to diabetic
				repeat (DR1)- like elements	neuropathy), blood vessel
				MEp and MEd identified as	blockage, heart disease, stroke,
				putative PPAR response	impotence (e.g., due to diabetic
				elements. ME promoter may	neuropathy or blood vessel
				also responds to AP1 and other	blockage), seizures, mental
_				transcription factors.	confusion, drowsiness,
				Exemplary assays that may be	nonketotic hyperglycemic-
				used or routinely modified to	hyperosmolar coma,
				test for regulation of	cardiovascular disease (e.g.,
				transcription of Malic Enzyme	heart disease, atherosclerosis,
				(in adipoocytes) by	microvascular disease,
				polypeptides of the invention	hypertension, stroke, and other
				(including antibodies and	diseases and disorders as

				agonists or antagonists of the	described in the
				invention) include assays	"Cardiovascular Disorders"
				disclosed in: Streeper, R.S., et	section below), dyslipidemia,
				al., Mol Endocrinol,	endocrine disorders (as
				12(11):1778-91 (1998);	described in the "Endocrine
				Garcia-Jimenez, C., et al., Mol	Disorders" section below),
				Endocrinol, 8(10):1361-9	neuropathy, vision impairment
				(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
				Biol Chem, 274(25):17997-	blindness), ulcers and impaired
				8004 (1999); Ijpenberg, A., et	wound healing, and infection
				al., J Biol Chem,	(e.g., infectious diseases and
				272(32):20108-20117 (1997);	disorders as described in the
				Berger, et al., Gene 66:1-10	"Infectious Diseases" section
				(1988); and, Cullen, B., et al.,	below, especially of the
				Methods in Enzymol.	urinary tract and skin), carpal
				216:362–368 (1992), the	tunnel syndrome and
				contents of each of which is	Dupuytren's contracture).
_				herein incorporated by	An additional highly preferred
				reference in its entirety.	indication is obesity and/or
				Hepatocytes that may be used	complications associated with
				according to these assays are	obesity. Additional highly
				publicly available (e.g.,	preferred indications include
				through the ATCC) and/or	weight loss or alternatively,
	_			may be routinely generated.	weight gain. Aditional
				Exemplary hepatocytes that	highly preferred indications are
				may be used according to these	complications associated with
_				assays includes the H4IIE rat	insulin resistance.
				liver hepatoma cell line.	
	HSDSB09	1443	SEAP in HIB/CRE		
495					
	HSDSB09	1443	Stimulation of	Assays for measuring calcium	A highly preferred

495		Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
		pancreatic beta	and may be used or routinely	An additional highly preferred
		cells.	modified to assess the ability	indication is a complication
			of polypeptides of the	associated with diabetes (e.g.,
			invention (including antibodies	diabetic retinopathy, diabetic
			and agonists or antagonists of	nephropathy, kidney disease
			the invention) to mobilize	(e.g., renal failure,
	-	_	calcium. For example, the	nephropathy and/or other
			FLPR assay may be used to	diseases and disorders as
			measure influx of calcium.	described in the "Renal
			Cells normally have very low	Disorders" section below),
			concentrations of cytosolic	diabetic neuropathy, nerve
			calcium compared to much	disease and nerve damage
			higher extracellular calcium.	(e.g., due to diabetic
			Extracellular factors can cause	neuropathy), blood vessel
			an influx of calcium, leading to	blockage, heart disease, stroke,
			activation of calcium	impotence (e.g., due to diabetic
			responsive signaling pathways	neuropathy or blood vessel
			and alterations in cell	blockage), seizures, mental
			functions. Exemplary assays	confusion, drowsiness,
-			that may be used or routinely	nonketotic hyperglycemic-
			modified to measure calcium	hyperosmolar coma,
			flux by polypeptides of the	cardiovascular disease (e.g.,
			invention (including antibodies	heart disease, atherosclerosis,
			and agonists or antagonists of	microvascular disease,
			the invention) include assays	hypertension, stroke, and other
			disclosed in: Satin LS, et al.,	diseases and disorders as
			Endocrinology, 136(10):4589-	described in the
			601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
			Endocrinology, 136(7):2960-6	section below), dyslipidemia,
			(1995); Richardson SB, et al.,	endocrine disorders (as

		Biochem J. 288 (Pt 3):847-51	described in the "Endocrine
		(1992); and, Meats, JÉ, et al.,	Disorders" section below),
		Cell Calcium 1989 Nov-	neuropathy, vision impairment
		Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
		contents of each of which is	blindness), ulcers and impaired
-		herein incorporated by	wound healing, and infection
		reference in its entirety.	(e.g., infectious diseases and
		Pancreatic cells that may be	disorders as described in the
		used according to these assays	"Infectious Diseases" section
	-	are publicly available (e.g.,	below, especially of the
		through the ATCC) and/or	urinary tract and skin), carpal
		may be routinely generated.	tunnel syndrome and
		Exemplary pancreatic cells that	Dupuytren's contracture).
		may be used according to these	An additional highly preferred
		assays include HITT15 Cells.	indication is obesity and/or
		HITT15 are an adherent	complications associated with
		epithelial cell line established	obesity. Additional highly
		from Syrian hamster islet cells	preferred indications include
		transformed with SV40. These	weight loss or alternatively,
		cells express glucagon,	weight gain. Aditional
		somatostatin, and	highly preferred indications are
		glucocorticoid receptors. The	complications associated with
		cells secrete insulin, which is	insulin resistance.
		stimulated by glucose and	
		glucagon and suppressed by	
		somatostatin or	
		glucocorticoids. ATTC# CRL-	
		1777 Refs: Lord and	
		Ashcroft. Biochem. J. 219:	
		547-551; Santerre et al. Proc.	
		Natl. Acad. Sci. USA 78:	

				4339-4343, 1981.	
	HSDSB09	1443	Activation of	This reporter assay measures	Highly preferred indications
495			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred
				through the GATA3 response	indications include neoplastic
				element that may be used or	diseases (e.g., leukemia,
				routinely modified to test	lymphoma, melanoma,
				GATA3-response element	prostate, breast, lung, colon,
				activity of polypeptides of the	pancreatic, esophageal,
				invention (including antibodies	stomach, brain, liver, and
				and agonists or antagonists of	urinary tract cancers and/or as

		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
		Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
		Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
		14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
		contents of each of which are	lymphoma, arthritis, AIDS,
		herein incorporated by	granulomatous disease,
		reference in its entirety. Mast	inflammatory bowel disease,
		cells that may be used	sepsis, neutropenia,
		according to these assays are	neutrophilia, psoriasis,
		publicly available (e.g.,	suppression of immune
		through the ATCC).	reactions to transplanted
		Exemplary human mast cells	organs and tissues, hemophilia,
		that may be used according to	hypercoagulation, diabetes
		these assays include the HMC-	mellitus, endocarditis,
		1 cell line, which is an	meningitis, and Lyme Disease.
		immature human mast cell line	
-		established from the peripheral	
		blood of a patient with mast	
		cell leukemia, and exhibits	
		many characteristics of	,

				immature mast cells.	
	HSDSB09	1443	Activation of	This reporter assay measures	Highly preferred indications
495			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic
				transcription through the	diseases (e.g., leukemia,
				NFAT response element that	lymphoma, melanoma,
				may be used or routinely	prostate, breast, lung, colon,
				modified to test NFAT-	pancreatic, esophageal,
				response element activity of	stomach, brain, liver, and
				polypeptides of the invention	urinary tract cancers and/or as

		-
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
 	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
	which are herein incorporated	sepsis, neutropenia,
	by reference in its entirety.	neutrophilia, psoriasis,
	Mast cells that may be used	suppression of immune
	according to these assays are	reactions to transplanted
	publicly available (e.g.,	organs and tissues, hemophilia,
	through the ATCC).	hypercoagulation, diabetes
	Exemplary human mast cells	mellitus, endocarditis,
	that may be used according to	meningitis, and Lyme Disease.
	these assays include the HMC-	
	1 cell line, which is an	
	immature human mast cell line	
	established from the peripheral	
	blood of a patient with mast	

				cell leukemia, and exhibits	
				many characteristics of	
	HSDSB09	1443	Activation of	This reporter assay measures	Highly preferred indication
495			transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in HMC-1	rhinitis. Additional highly
			response element in	human mast cell line.	preferred indications include
			immune cells (such	Activation of NFkB in mast	infection (e.g., an infectious
			as mast cells).	cells has been linked to	disease as described below
				production of certain	under "Infectious Disease"),
				cytokines, such as IL-6 and IL-	and inflammation and
				9. Assays for the activation of	inflammatory disorders.
				transcription through the	Preferred indications include
				NFKB response element are	immunological and
				well-known in the art and may	hempatopoietic disorders (e.g.,
				be used or routinely modified	as described below under
				to assess the ability of	"Immune Activity", and
				polypeptides of the invention	"Blood-Related Disorders").
				(including antibodies and	Preferred indications also
				agonists or antagonists of the	include autoimmune diseases
				invention) to regulate NFKB	(e.g., rheumatoid arthritis,
				transcription factors and	systemic lupus erythematosis,
				modulate expression of	multiple sclerosis and/or as
				immunomodulatory genes.	described below) and
				Exemplary assays for	immunodeficiencies (e.g., as
				transcription through the	described below). Preferred
				NFKB response element that	indications also include
				may be used or rountinely	neoplastic diseases (e.g.,
				modified to test NFKB-	leukemia, lymphoma,
				response element activity of	melanoma, and/or as described
				polypeptides of the invention	below under

			(including antibodies and	"Hyperproliferative
			agonists or antagonists of the	Disorders"). Preferred
			invention) include assays	indications include neoplasms
			disclosed in Berger et al., Gene	and cancer, such as, for
	-		66:1-10 (1998); Cullen and	example, leukemia, lymphoma,
	-		Malm, Methods in Enzymol	melanoma, and prostate,
		-	216:362-368 (1992); Henthorn	breast, lung, colon, pancreatic,
			et al., Proc Natl Acad Sci USA	esophageal, stomach, brain,
			85:6342-6346 (1988); Stassen	liver, urinary tract cancers and
			et al, J Immunol 166(7):4391-8	as described below under
			(2001); and Marquardt and	"Hyperproliferative
			Walker, J Allergy Clin	Disorders".
			Immunol 105(3):500-5 (2000),	
			the contents of each of which	
			are herein incorporated by	
			reference in its entirety. Mast	
		18.0	cells that may be used	
			according to these assays are	
			publicly available (e.g.,	
			through the ATCC).	
			Exemplary human mast cells	
****	_		that may be used according to	
			these assays include the HMC-	
			1 cell line, which is an	
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
!	!	!	immature mast cells.	
HSDSB09	1443	Activation of	Assays for the activation of	Highly preferred indications

495	transcription	transcription through the	include allergy, asthma, and
	through STAT6	Signal Transducers and	rhinitis. Additional highly
	response element in	Activators of Transcription	preferred indications include
	immune cells (such	(STAT6) response element in	infection (e.g., an infectious
	as mast cells).	immune cells (such as in the	disease as described below
		human HMC-1 mast cell line)	under "Infectious Disease"),
		are well-known in the art and	and inflammation and
		may be used or routinely	inflammatory disorders.
		modified to assess the ability	Preferred indications also
		of polypeptides of the	include hematopoietic and
		invention (including antibodies	immunological disorders (e.g.,
		and agonists or antagonists of	as described below under
		the invention) to regulate	"Immune Activity", "Blood-
		STAT6 transcription factors	Related Disorders", and/or
		and modulate the expression of	"Cardiovascular Disorders"),
		multiple genes. Exemplary	autoimmune diseases (e.g.,
		assays for transcription	rheumatoid arthritis, systemic
		through the STAT6 response	lupus erythematosis, multiple
		element that may be used or	sclerosis and/or as described
		routinely modified to test	below), and
		STAT6 response element	immunodeficiencies (e.g., as
		activity of the polypeptides of	described below). Preferred
		the invention (including	indications include neoplastic
		antibodies and agonists or	diseases (e.g., leukemia,
		antagonists of the invention)	lymphoma, melanoma, and/or
		include assays disclosed in	as described below under
		Berger et al., Gene 66:1-10	"Hyperproliferative
		(1998); Cullen and Malm,	Disorders"). Preferred
		Methods in Enzymol 216:362-	indications include neoplasms
		368 (1992); Henthorn et al.,	and cancer, such as, for
		Proc Natl Acad Sci USA	example, leukemia, lymphoma,

				85:6342-6346 (1988);	melanoma, and prostate,
				Sherman, Immunol Rev	breast, lung, colon, pancreatic,
				179:48-56 (2001); Malaviya	esophageal, stomach, brain,
				and Uckun, J Immunol	liver and urinary cancer. Other
				168:421-426 (2002); Masuda	preferred indications include
				et al., J Biol Chem	benign dysproliferative
				275(38):29331-29337 (2000);	disorders and pre-neoplastic
				and Masuda et al., J Biol Chem	conditions, such as, for
				276:26107-26113 (2001), the	example, hyperplasia,
				contents of each of which are	metaplasia, and/or dysplasia.
				herein incorporated by	Preferred indications include
				reference in its entirety. Mast	hematopoietic and
		-		cells that may be used	immunological disorders such
				according to these assays are	as arthritis, AIDS,
				publicly available (e.g.,	granulomatous disease,
				through the ATCC).	inflammatory bowel disease,
				Exemplary human mast cells	sepsis, neutropenia,
				that may be used according to	neutrophilia, psoriasis,
				these assays include the HMC-	suppression of immune
				1 cell line, which is an	reactions to transplanted
				immature human mast cell line	organs and tissues, hemophilia,
				established from the peripheral	hypercoagulation, diabetes
				blood of a patient with mast	mellitus, endocarditis,
				cell leukemia, and exhibits	meningitis, and Lyme Disease.
				many characteristics of	
				immature mast cells.	
495	HSDSB09	1443	CXCR4 in HT1080		
495	HSDSB09	1443	IgG in Human B		
	HSDSB09	1443	IgG in Human B		

495			cells SAC		
	HSDSB09	1443	Stimulation of	Assays for measuring secretion	A highly preferred
495			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
				cells) by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other
				disclosed in: Ahren, B., et al.,	diseases and disorders as
				Am J Physiol, 277(4 Pt	described in the
				2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"

				ol Endoominology	andinibal during
				129(0):2725 40 (1007): V:	section octow), at surpraeming,
				138(9):3/33-40 (1997); NIM,	endocrine disorders (as
				K.H., et al., FEBS Lett,	described in the "Endocrine
				377(2):237-9 (1995); and,	Disorders" section below),
				Miraglia S et. al., Journal of	neuropathy, vision impairment
				Biomolecular Screening,	(e.g., diabetic retinopathy and
				4:193-204 (1999), the contents	blindness), ulcers and impaired
				of each of which is herein	wound healing, and infection
				incorporated by reference in its	(e.g., infectious diseases and
				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
-				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:16/.	
105	HSDSB09	1443	SEAP in Jurkat/IL4		
47.7			promoter		

	HSDSB09	1443	SEAP in Jurkat/IL4		
495			promoter (antiCD3 co-stim)		
	HSDSB09	1443	Activation of	This reporter assay measures	Highly preferred indication
495			transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in Ku812	rhinitis. Additional highly
			response element in	human basophil cell line.	preferred indications include
			immune cells (such	Assays for the activation of	infection (e.g., an infectious
			as basophils).	transcription through the	disease as described below
				NFKB response element are	under "Infectious Disease"),
				well-known in the art and may	and inflammation and
				be used or routinely modified	inflammatory disorders.
				to assess the ability of	Preferred indications include
				polypeptides of the invention	immunological and
				(including antibodies and	hempatopoietic disorders (e.g.,
				agonists or antagonists of the	as described below under
				invention) to regulate NFKB	"Immune Activity", and
				transcription factors and	"Blood-Related Disorders").
				modulate expression of	Preferred indications also
				immunomodulatory genes.	include autoimmune diseases
				Exemplary assays for	(e.g., rheumatoid arthritis,
				transcription through the	systemic lupus erythematosis,
				NFKB response element that	multiple sclerosis and/or as
				may be used or rountinely	described below) and
				modified to test NFKB-	immunodeficiencies (e.g., as
				response element activity of	described below). Preferred
				polypeptides of the invention	indications also include
				(including antibodies and	neoplastic diseases (e.g.,
_				agonists or antagonists of the	leukemia, lymphoma,
				invention) include assays	melanoma, and/or as described
				disclosed in Berger et al., Gene	below under

				66:1-10 (1998); Cullen and	"Hyperproliferative
				Malm, Methods in Enzymol	Disorders"). Preferred
				216:362-368 (1992); Henthorn	indications include neoplasms
				et al., Proc Natl Acad Sci USA	and cancer, such as, for
				85:6342-6346 (1988); Marone	example, leukemia, lymphoma,
				et al, Int Arch Allergy	melanoma, and prostate,
				Immunol 114(3):207-17	breast, lung, colon, pancreatic,
				(1997), the contents of each of	esophageal, stomach, brain,
				which are herein incorporated	liver, urinary tract cancers and
				by reference in its entirety.	as described below under
				Basophils that may be used	"Hyperproliferative
				according to these assays are	Disorders".
				publicly available (e.g.,	
				through the ATCC).	
				Exemplary human basophil	
				cell lines that may be used	
				according to these assays	
				include Ku812, originally	
				established from a patient with	
				chronic myelogenous	
				leukemia. It is an immature	
		_		prebasophilic cell line that can	
				be induced to differentiate into	
	HSDSB09	1443	SEAP in		
495			Ku812/NFkB (TNF		
			synergy)		
	HSDSB09	1443	Activation of	Assays for the activation of	A preferred embodiment of
495			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha

immine cells (such	art and may be used or	production. An alternative
as natural killer	routinely modified to assess	highly preferred embodiment
 cells).	the ability of polypeptides of	of the invention includes a
	the invention (including	method for stimulating (e.g.,
	antibodies and agonists or	increasing) TNF alpha
	antagonists of the invention) to	production. Preferred
	regulate serum response	indications include blood
	factors and modulate the	disorders (e.g., as described
	expression of genes involved	below under "Immune
	in growth and upregulate the	Activity", "Blood-Related
	function of growth-related	Disorders", and/or
	genes in many cell types.	"Cardiovascular Disorders"),
	Exemplary assays for	Highly preferred indications
	transcription through the SRE	include autoimmune diseases
	that may be used or routinely	(e.g., rheumatoid arthritis,
	modified to test SRE activity	systemic lupus erythematosis,
	of the polypeptides of the	Crohn"s disease, multiple
	invention (including antibodies	sclerosis and/or as described
	and agonists or antagonists of	below), immunodeficiencies
	the invention) include assays	(e.g., as described below),
	disclosed in Berger et al., Gene	boosting a T cell-mediated
	66:1-10 (1998); Cullen and	immune response, and
	Malm, Methods in Enzymol	suppressing a T cell-mediated
	216:362-368 (1992); Henthorn	immune response. Additional
	et al., Proc Natl Acad Sci USA	highly preferred indications
	85:6342-6346 (1988); Benson	include inflammation and
	et al., J Immunol 153(9):3862-	inflammatory disorders, and
	3873 (1994); and Black et al.,	treating joint damage in
	Virus Genes 12(2):105-117	patients with rheumatoid
	(1997), the content of each of	arthritis. An additional highly
	which are herein incorporated	preferred indication is sepsis.

AG	by reference in its entirety. T	Highly preferred indications
	cells that may be used	include neoplastic diseases
acc	according to these assays are	(e.g., leukemia, lymphoma,
Ind	publicly available (e.g.,	and/or as described below
thre	through the ATCC).	under "Hyperproliferative
Exe	Exemplary T cells that may be	Disorders"). Additionally,
esn	used according to these assays	highly preferred indications
inc	lude the NK-YT cell line,	include neoplasms and
hw wh	which is a human natural killer	cancers, such as, for example,
[lea]	cell line with cytolytic and	leukemia, lymphoma,
cyt	cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
	!	disease, inflammatory bowel

					disease neutronenia
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
		-			meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HSDSB09	1443	Activation of	Assays for the activation of	A highly preferred
495			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
			response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
			as T-cells).	well-known in the art and may	indications include
				be used or routinely modified	inflammation and
				to assess the ability of	inflammatory disorders.
				polypeptides of the invention	Preferred indications include
		_		(including antibodies and	blood disorders (e.g., as
				agonists or antagonists of the	described below under
				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
				modulate the expression of	"Cardiovascular Disorders").
				multiple genes. Exemplary	Preferred indications include
				assays for transcription	autoimmune diseases (e.g.,
				through the STAT6 response	rheumatoid arthritis, systemic

element that may be used or	lupus erythematosis, multiple
routinely modified to test	sclerosis and/or as described
 STAT6 response element	below) and
activity of the polypeptides of	immunodeficiencies (e.g., as
the invention (including	described below).
antibodies and agonists or	Preferred indications include
antagonists of the invention)	neoplastic diseases (e.g.,
include assays disclosed in	leukemia, lymphoma,
Berger et al., Gene 66:1-10	melanoma, and/or as described
(1998); Cullen and Malm,	below under
Methods in Enzymol 216:362-	"Hyperproliferative
368 (1992); Henthorn et al.,	Disorders"). Preferred
Proc Natl Acad Sci USA	indications include neoplasms
85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
(1998); Moffatt et al.,	prostate, breast, lung, colon,
Transplantation $69(7)$ :1521-	pancreatic, esophageal,
1523 (2000); Curiel et al., Eur	stomach, brain, liver and
J Immunol 27(8):1982-1987	urinary cancer. Other preferred
(1997); and Masuda et al., J	indications include benign
Biol Chem 275(38):29331-	dysproliferative disorders and
29337 (2000), the contents of	pre-neoplastic conditions, such
each of which are herein	as, for example, hyperplasia,
incorporated by reference in its	metaplasia, and/or dysplasia.
entirety. T cells that may be	Preferred indications include
used according to these assays	anemia, pancytopenia,
are publicly available (e.g.,	leukopenia, thrombocytopenia,
through the ATCC).	Hodgkin's disease, acute
Exemplary T cells that may be	lymphocytic anemia (ALL),
used according to these assays	plasmacytomas, multiple
include the SUPT cell line,	myeloma, Burkitt's lymphoma,

				which is a suspension culture	arthritis, AIDS, granulomatous
				of IL-2 and IL-4 responsive T	disease, inflammatory bowel
				cells.	disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additional preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
495	HSDSB09	1443	CXCR4 in SW480		
	HSDSE75	1444	Myoblast cell	Assays for muscle cell	Highly preferred indications
496			proliferation	proliferation are well known in	include diabetes, myopathy,
				the art and may be used or	muscle cell atrophy, cancers of
				routinely modified to assess	muscle (such as,
				the ability of polypeptides of	rhabdomyoma, and
				the invention (including	rhabdosarcoma),
				antibodies and agonists or	cardiovascular disorders (such
				antagonists of the invention) to	as congestive heart failure,
				stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
				cell proliferation. Exemplary	congenital cardiovascular
				assays for myoblast cell	abnormalities, heart disease,
				proliferation that may be used	cardiac arrest, heart valve
				or routinely modified to test	disease, vascular disease, and
				activity of polypeptides and	also as described below under

								-																
"Cardiovascular Disorders"), stimulating myoblast proliferation, and inhibiting	myoblast proliferation.																							
antibodies of the invention (including agonists or antagonists of the invention)	include, for example, assays disclosed in: Soeta, C., et al.	gene in the proliferation of	myogenic cells in regenerating skeletal muscles of rats" Dev	Growth Differ Apr;43(2):155-	"IGF binding proteins-4, -5	and -6 may play specialized	roles during L6 myoblast	proliferation and	differentiation" J Endocrinol	Mar;144(3):539-53 (1995);	and, Pampusch MS, et	al.,"Effect of transforming	growth factor beta on	proliferation of L6 and	embryonic porcine myogenic	cells" J Cell Physiol	Jun;143(3):524-8 (1990); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary myoblast cells that	may be used according to these	assays include the rat myoblast	L6 cell line. Rat myoblast L6
										-														

				cells are an adherent rat	
				myoblast cell line, isolated	
				from primary cultures of rat	
				thigh muscle, that fuse to form	
				multinucleated myotubes and	
				striated fibers after culture in	
				differentiation media.	
	HSDSE75	1444	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
496				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
•		<del></del>		disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
		·		Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic

	(including antibodies and	limis erythematosis multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders. Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	 (including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,

				by reference in its entirety.	stomach, brain, liver and
				Human dendritic cells that may	urinary cancer. Other preferred
				be used according to these	indications include benign
<u> </u>				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
_	· <u></u>	-		antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
497	HSDZR57	1445	SEAP in Alk Phos C2C12		

	HSDZR57	1445	SEAP in ATP-3T3-		
497			L1		
	HSDZR57	1445	Activation of	Kinase assay. JNK and p38	A highly preferred
497			Endothelial Cell	kinase assays for signal	embodiment of the invention
	-		p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred
				antibodies and agonists or	embodiment of the invention
				antagonists of the invention) to	includes a method for
				promote or inhibit cell	stimulating endothelial cell
				proliferation, activation, and	proliferation. An alternative
				apoptosis. Exemplary assays	highly preferred embodiment
				for JNK and p38 kinase	of the invention includes a
				activity that may be used or	method for inhibiting
				routinely modified to test JNK	endothelial cell proliferation.
-		-		and p38 kinase-induced	A highly preferred
				activity of polypeptides of the	embodiment of the invention
				invention (including antibodies	includes a method for
-				and agonists or antagonists of	stimulating apoptosis of
				the invention) include the	endothelial cells. An
				assays disclosed in Forrer et	alternative highly preferred
				al., Biol Chem 379(8-9):1101-	embodiment of the invention
				1110 (1998); Gupta et al., Exp	includes a method for
				Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
				(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
				Soc Symp 64:29-48 (1999);	A highly preferred
				Chang and Karin, Nature	embodiment of the invention

410(6824):37-40 (2001); and	includes a method for
Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
 the contents of each of which	alternative highly preferred
are herein incorporated by	embodiment of the invention
reference in its entirety.	includes a method for
Endothelial cells that may be	inhibiting (e.g., decreasing) the
used according to these assays	activation of and/or
are publicly available (e.g.,	inactivating endothelial cells.
through the ATCC).	A highly preferred
 Exemplary endothelial cells	embodiment of the invention
that may be used according to	includes a method for
 these assays include human	stimulating angiogenisis. An
umbilical vein endothelial cells	
 (HUVEC), which are	embodiment of the invention
endothelial cells which line	includes a method for
venous blood vessels, and are	inhibiting angiogenesis. A
involved in functions that	highly preferred embodiment
include, but are not limited to,	of the invention includes a
angiogenesis, vascular	method for reducing cardiac
 permeability, vascular tone,	hypertrophy. An alternative
and immune cell extravasation.	highly preferred embodiment
	of the invention includes a
	method for inducing cardiac
	hypertrophy. Highly
	preferred indications include
	neoplastic diseases (e.g., as
	described below under
	"Hyperproliferative
	Disorders"), and disorders of
	the cardiovascular system

(e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis	and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or	as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as	themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.  Highly preferred indications

	to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangiosarcoma. Highly
	leukemias, and Kaposi"s sarcoma, and retinal disorde Highly preferred indications include neoplasms and canc such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangiosarcoma. Highl
	sarcoma, and retinal disorde Highly preferred indications include neoplasms and canc such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, lymphangiosarcoma, lymphangiosarcoma, lymphangiosarcoma. Highl
	Highly preferred indications include neoplasms and canc such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangiosarcoma. Highl
	include neoplasms and canc such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangiosarcoma, Highl
	such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangiosarcoma. Highl
	hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highl
	cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highl
	telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highl
	angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highl
	hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highl
	angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highl
	haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highl
	lymphangioma, lymphangiosarcoma. Highl
	lymphangiosarcoma. Highl
_	
	preferred indications also
	include cancers such as,
	prostate, breast, lung, colon,
	pancreatic, esophageal,
	stomach, brain, liver, and
	urinary cancer. Preferred
	indications include benign
	dysproliferative disorders and
	pre-neoplastic conditions, such
	as, for example, hyperplasia,
	metaplasia, and/or dysplasia.
	Highly preferred indications
	also include arterial disease,
	such as, atherosclerosis,
	hypertension, coronary artery

disease inflammatory	vasculitides. Revnaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	Iymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	
																													_

angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions.  Additional highly preferred indications include fibromas	heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include	described below under "Immune Activity", "Blood- Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such	as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain
	·				

					management.
	HSHAX21	1446	Activation of	Kinase assay. Kinase assays,	A highly preferred
498			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
			-	inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
			_	test ERK kinase-induced	differentiation. A highly
				activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
				and agonists or antagonists of	for stimulating (e.g.,
				the invention) include the	increasing) adipocyte
				assays disclosed in Forrer et	activation. An alternative
				al., Biol Chem 379(8-9):1101-	highly preferred embodiment
				1110 (1998); Le Marchand-	of the invention includes a
				Brustel Y, Exp Clin	method for inhibiting the
				Endocrinol Diabetes	activation of (e.g., decreasing)
				107(2):126-132 (1999);	and/or inactivating adipocytes.
				Kyriakis JM, Biochem Soc	Highly preferred indications
				Symp 64:29-48 (1999); Chang	include endocrine disorders

		and Karin. Nature	(e.g., as described below under
		410(6824):37-40 (2001); and	"Endocrine Disorders").
		Cobb MH, Prog Biophys Mol	Highly preferred indications
		Biol 71(3-4):479-500 (1999);	also include neoplastic
		the contents of each of which	diseases (e.g., lipomas,
	-	are herein incorporated by	liposarcomas, and/or as
		reference in its entirety.	described below under
		Mouse adipocyte cells that	"Hyperproliferative
		may be used according to these	Disorders"). Preferred
		assays are publicly available	indications include blood
		(e.g., through the ATCC).	disorders (e.g., hypertension,
		Exemplary mouse adipocyte	congestive heart failure, blood
		cells that may be used	vessel blockage, heart disease,
		according to these assays	stroke, impotence and/or as
		include 3T3-L1 cells. 3T3-L1	described below under
		is an adherent mouse	"Immune Activity",
		preadipocyte cell line that is a	"Cardiovascular Disorders",
		continuous substrain of 3T3	and/or "Blood-Related
		fibroblast cells developed	Disorders"), immune disorders
		through clonal isolation and	(e.g., as described below under
		undergo a pre-adipocyte to	"Immune Activity"), neural
		adipose-like conversion under	disorders (e.g., as described
		appropriate differentiation	below under "Neural Activity
		conditions known in the art.	and Neurological Diseases"),
			and infection (e.g., as
			described below under
			"Infectious Disease").
			A highly preferred indication
	-		is diabetes mellitus. An
			additional highly preferred
			indication is a complication

associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure,	diseases and disorders as described in the "Renal	diabetic neuropathy, nerve disease and nerve damage	neuropathy), blood vessel blockage, heart disease, stroke,	impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental	confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma,	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the	"Cardiovascular Disorders" section below), dyslipidemia,	described in the "Endocrine Disorders" section below),

(e.g., diabetic retinopathy and
blindness), ulcers and impaired
wound healing, infection (e.g.,
infectious diseases and
disorders as described in the
"Infectious Diseases" section
below (particularly of the
urinary tract and skin). An
additional highly preferred
indication is obesity and/or
complications associated with
obesity. Additional highly
preferred indications include
weight loss or alternatively,
weight gain. Additional
highly preferred indications are
complications associated with
 insulin resistance.
Additional highly preferred
indications are disorders of the
musculoskeletal systems
including myopathies,
muscular dystrophy, and/or as
 described herein.
Additional highly preferred
indications include,
hypertension, coronary artery
 disease, dyslipidemia,
 gallstones, osteoarthritis,
degenerative arthritis, eating
disorders, fibrosis, cachexia,

					and kidney diseases or
					die ment de la constant
					disorders. Preferred
					indications include neoplasms
					and cancer, such as,
		**			lymphoma, leukemia and
					breast, colon, and kidney
					cancer. Additional preferred
					indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HSHAX21	1446	Production of	MIP-1alpha FMAT. Assays	A highly preferred
498			MIP1alpha	for immunomodulatory	embodiment of the invention
				proteins produced by activated	includes a method for
				dendritic cells that upregulate	stimulating MIP1a production.
				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well	embodiment of the invention
				known in the art and may be	includes a method for
				used or routinely modified to	inhibiting (e.g., reducing)
				assess the ability of	MIP1a production. A highly
				polypeptides of the invention	preferred indication is
				(including antibodies and	infection (e.g., an infectious
				agonists or antagonists of the	disease as described below

ui	invention) to mediate	under "Infectious Disease").
 ni .	immunomodulation, modulate	Preferred indications include
- ch	chemotaxis, and modulate T	blood disorders (e.g., as
 93	cell differentiation. Exemplary	described below under
as	assays that test for	"Immune Activity", "Blood-
ii	immunomodulatory proteins	Related Disorders", and/or
· ev	evaluate the production of	"Cardiovascular Disorders").
ch	chemokines, such as	Highly preferred indications
	macrophage inflammatory	include autoimmune diseases
nd	protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
	the activation of	systemic lupus erythematosis,
 ш	monocytes/macrophages and T	multiple sclerosis and/or as
3	cells. Such assays that may be	described below) and
sn	used or routinely modified to	immunodeficiencies (e.g., as
te	test immunomodulatory and	described below). Additional
ch	chemotaxis activity of	highly preferred indications
bc	polypeptides of the invention	include inflammation and
<u></u>	(including antibodies and	inflammatory disorders.
a	agonists or antagonists of the	Preferred indications also
ni	invention) include assays	include anemia, pancytopenia,
 - di	disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
 B	Biomolecular Screening 4:193-	Hodgkin's disease, acute
20	204(1999); Rowland et al.,	lymphocytic anemia (ALL),
1	"Lymphocytes: a practical	plasmacytomas, multiple
ap	approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,
(2	(2000); Satthaporn and	arthritis, AIDS, granulomatous
 <u> </u>	Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
45	45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
 al	al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
29	29 (2000); Verhasselt et al., J	suppression of immune
 ll In	Immunol 158: 2919-2925	reactions to transplanted

				(1997); and Nardelli et al., J	organs and tissues, hemophilia,
				Leukoc Biol 65:822-828	hypercoagulation, diabetes
				(1999), the contents of each of	mellitus, endocarditis,
				which are herein incorporated	meningitis, Lyme Disease,
				by reference in its entirety.	asthma, and allergy.
				Human dendritic cells that may	Preferred indications also
				be used according to these	include neoplastic diseases
				assays may be isolated using	(e.g., leukemia, lymphoma,
				techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
		•		antigen presenting cells in	indications include neoplasms
				suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
				and/or cytokines, initiate and	lung, colon, pancreatic,
				upregulate T cell proliferation	esophageal, stomach, brain,
				and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HSHAX21	1446	Production of TNF	TNFa FMAT. Assays for	A highly preferred
498			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for

	variety of cells are well known	stimulatino (e o increasino)
	in the art and may be used or	TNF alpha production.
	routinely modified to assess	Highly preferred indications
	the ability of polypeptides of	include blood disorders (e.g.,
	the invention (including	as described below under
	antibodies and agonists or	"Immune Activity", "Blood-
	antagonists of the invention) to	Related Disorders", and/or
	mediate immunomodulation,	"Cardiovascular Disorders"),
	modulate inflammation and	Highly preferred indications
	cytotoxicity. Exemplary	include autoimmune diseases
	assays that test for	(e.g., rheumatoid arthritis,
	immunomodulatory proteins	systemic lupus erythematosis,
	evaluate the production of	Crohn"s disease, multiple
	cytokines such as tumor	sclerosis and/or as described
	necrosis factor alpha (TNFa),	below), immunodeficiencies
	and the induction or inhibition	(e.g., as described below),
	of an inflammatory or	boosting a T cell-mediated
	cytotoxic response. Such	immune response, and
	assays that may be used or	suppressing a T cell-mediated
	routinely modified to test	immune response. Additional
	immunomodulatory activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders, and
	agonists or antagonists of the	treating joint damage in
	invention) include assays	patients with rheumatoid
	disclosed in Miraglia et al., J	arthritis. An additional highly
	Biomolecular Screening 4:193-	preferred indication is sepsis.
	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases
	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); Verhasselt et al., Eur J	and/or as described below

Immi	Immunol 28(11):3886-3890	under "Hyperproliferative
(1198	(1198); Dahlen et al., J	Disorders"). Additionally,
Immi	Immunol 160(7):3585-3593	highly preferred indications
8661)	(1998); Verhasselt et al., J	include neoplasms and
nmul	Immunol 158:2919-2925	cancers, such as, leukemia,
 (1997	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
Leuk	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
(1999)	(1999), the contents of each of	tumors, and prostate, breast,
which	which are herein incorporated	lung, colon, pancreatic,
by red	by reference in its entirety.	esophageal, stomach, brain,
Hum	Human dendritic cells that may	liver and urinary cancer. Other
 pe us	be used according to these	preferred indications include
assay	assays may be isolated using	benign dysproliferative
techn	techniques disclosed herein or	disorders and pre-neoplastic
other	otherwise known in the art.	conditions, such as, for
Hnm	Human dendritic cells are	example, hyperplasia,
antige	antigen presenting cells in	metaplasia, and/or dysplasia.
edsns	suspension culture, which,	Preferred indications include
when	when activated by antigen	anemia, pancytopenia,
and/o	and/or cytokines, initiate and	leukopenia, thrombocytopenia,
upreg	upregulate T cell proliferation	Hodgkin's disease, acute
and fi	and functional activities.	lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
	!	organs and tissues,

					hamonhilia hunarooganlation
					dishator malliture and countities
					diabetes meinius, endocardius,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
-					disease as described below
					under "Infectious Disease").
	HSHAX21	1446	Activation of	Assays for the activation of	Highly preferred indications
498			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").

	invention) include assays	Highly preferred indications
	disclosed in Berger et al., Gene	include neoplastic diseases
-	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
	Malm, Methods in Enzymol	lymphoma, and/or as described
	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Gnes 15(2):105-117	indications include neoplasms
	(1997); and Fraser et al.,	and cancers, such as, for
	29(3):838-844 (1999), the	example, melanoma, renal cell
 	contents of each of which are	carcinoma, leukemia,
 	herein incorporated by	lymphoma, and prostate,
	reference in its entirety.	breast, lung, colon, pancreatic,
	Exemplary human T cells,	esophageal, stomach, brain,
_	such as the MOLT4, that may	liver and urinary cancer. Other
	be used according to these	preferred indications include
	assays are publicly available	benign dysproliferative
	(e.g., through the ATCC).	disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications also
		include anemia, pancytopenia,
 		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
 		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, sepsis, neutropenia,

					neutrophilia, psoriasis,
					hemonhilia hynercoaoulation
					diabetes mellitus, endocarditis.
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HSIAS17	1447	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
499				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
	_			myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic

(in	(including antibodies and	lupus erythematosis, multiple
ago	agonists or antagonists of the	sclerosis and/or as described
ni	invention) to mediate	below) and
·mi	immunomodulation and	immunodeficiencies (e.g., as
dif	differentiation and modulate T	described below). Highly
cel	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
imi	immunomodulatory proteins	mediated immune response
ev.	evaluate the production of	and alternatively suppressing a
cyt	cytokines, such as IL-6, and	B cell-mediated immune
the	the stimulation and	response. Highly preferred
ıdn	upregulation of T cell	indications include
out   but	proliferation and functional	inflammation and
act	activities. Such assays that	inflammatory
ma	may be used or routinely	disorders.Additional highly
om   mc	modified to test	preferred indications include
imi	immunomodulatory and	asthma and allergy. Highly
dif	diffferentiation activity of	preferred indications include
od	polypeptides of the invention	neoplastic diseases (e.g.,
(in	(including antibodies and	myeloma, plasmacytoma,
ago	agonists or antagonists of the	leukemia, lymphoma,
ni	invention) include assays	melanoma, and/or as described
dis	disclosed in Miraglia et al., J	below under
Bic	Biomolecular Screening 4:193-	"Hyperproliferative
20	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
api	approach" Chapter 6:138-160	and cancers, such as, myeloma,
(20	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
m I I I I I I I I I I I I I I I I I I I	Immunol 158:2919-2925	lymphoma, melanoma, and
(15)	(1997), the contents of each of	prostate, breast, lung, colon,
wh	which are herein incorporated	pancreatic, esophageal,

				by reference in its entirety.	stomach, brain, liver and
				Human dendritic cells that may	urinary cancer. Other preferred
				be used according to these	indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
<del>-</del>				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
			-	and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HSIAS17	1447	Production of TNF	TNFa FMAT. Assays for	A highly preferred
499			alpha by dendritic	immunomodulatory proteins	embodiment of the invention

includes a method for	inhibiting (e.g., decreasing)	e,   TNF alpha production. An	xert a alternative highly preferred	tory embodiment of the invention	includes a method for		for TNF alpha production.			as described below under		on) to Related Disorders", and/or	on, "Cardiovascular Disorders"),	nd Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,		f Crohn"s disease, multiple	sclerosis and/or as described			boosting a T cell-mediated	-	r suppressing a T cell-mediated		ity of   highly preferred indications	tion include inflammation and	inflammatory disorders, and	the treating joint damage in	patients with rheumatoid
produced by activated	macrophages, T cells,	fibroblasts, smooth muscle,	and other cell types that exert a	wide variety of inflammatory	and cytotoxic effects on a	variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays
cells																														
				_										_					_								-	-		

disclosed in Miraølia et al I	arthritis. An additional highly
Biomolecular Screening 4:193-	preferred indication is sensis.
204(1999); Rowland et al.,	Highly preferred indications
"Lymphocytes: a practical	include neoplastic diseases
approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
(2000); Verhasselt et al., Eur J	and/or as described below
Immunol 28(11):3886-3890	under "Hyperproliferative
(1198); Dahlen et al., J	Disorders"). Additionally,
Immunol 160(7):3585-3593	highly preferred indications
(1998); Verhasselt et al., J	include neoplasms and
Immunol 158:2919-2925	cancers, such as, leukemia,
(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
(1999), the contents of each of	tumors, and prostate, breast,
which are herein incorporated	lung, colon, pancreatic,
by reference in its entirety.	esophageal, stomach, brain,
Human dendritic cells that may	liver and urinary cancer. Other
be used according to these	preferred indications include
assays may be isolated using	benign dysproliferative
techniques disclosed herein or	disorders and pre-neoplastic
otherwise known in the art.	conditions, such as, for
Human dendritic cells are	example, hyperplasia,
antigen presenting cells in	metaplasia, and/or dysplasia.
suspension culture, which,	Preferred indications include
when activated by antigen	anemia, pancytopenia,
and/or cytokines, initiate and	leukopenia, thrombocytopenia,
upregulate T cell proliferation	Hodgkin's disease, acute
and functional activities.	lymphocytic anemia (ALL),
	plasmacytomas, multiple
	myeloma, Burkitt's lymphoma,
	arthritis, AIDS, granulomatous

					disease, inflammatory bowel disease, neutropenia,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia, hypercoagulation,
-					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
	_				is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
499	HSIAS17	1447	TNFa in Human T-cell 2B9		
	HSIAS17	1447	MCP-1 in HUVEC		
499					
	HSICV24	1448	Activation of	This reporter assay measures	Highly preferred indications
200			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under

<u> </u>	known in the art and may be	"Immune Activity", "Blood-
in	used or routinely modified to	Related Disorders", and/or
as	assess the ability of	"Cardiovascular Disorders").
jd .	polypeptides of the invention	Preferred indications include
<u></u>	(including antibodies and	autoimmune diseases (e.g.,
	agonists or antagonists of the	rheumatoid arthritis, systemic
ui.	invention) to regulate NFAT	lupus erythematosis, multiple
	transcription factors and	sclerosis and/or as described
m	modulate expression of genes	below) and
 ui	involved in	immunodeficiencies (e.g., as
ni	immunomodulatory functions.	described below). Preferred
—————————————————————————————————————	Exemplary assays for	indications include neoplastic
- tr	transcription through the	diseases (e.g., leukemia,
Z	NFAT response element that	lymphoma, melanoma,
u -	may be used or routinely	prostate, breast, lung, colon,
<u> </u>	modified to test NFAT-	pancreatic, esophageal,
re	response element activity of	stomach, brain, liver, and
)d	polypeptides of the invention	urinary tract cancers and/or as
<u>.i.)</u>	(including antibodies and	described below under
 	agonists or antagonists of the	"Hyperproliferative
ui	invention) include assays	Disorders"). Other preferred
- T	disclosed in Berger et al., Gene	indications include benign
 <del>)</del>	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
 5.2	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
<del>∞</del>	85:6342-6346 (1988); De Boer	Preferred indications include
et	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
3	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et	et al., J Immunol	leukemias, Hodgkin's disease,
10	165(12):7215-7223 (2000);	acute lymphocytic anemia

				Hutchinson and McCloskey, J	(ALL), plasmacytomas,
				Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HSIDJ81	1449	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
501				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred
				routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as

is measured by FMAT using	y FMAT using	described in the "Renal
anti-rat insulin antibodies.	antibodies.	Disorders" section below),
Insulin secretion from	on from	diabetic neuropathy, nerve
pancreatic beta cells is	a cells is	disease and nerve damage
upregulated by glucose and	glucose and	(e.g., due to diabetic
also by certain		neuropathy), blood vessel
proteins/peptides, and	des, and	blockage, heart disease, stroke,
disregulation is a key	s a key	impotence (e.g., due to diabetic
component in diabetes.	diabetes.	neuropathy or blood vessel
Exemplary ass	Exemplary assays that may be	blockage), seizures, mental
used or routine	used or routinely modified to	confusion, drowsiness,
test for stimula	test for stimulation of insulin	nonketotic hyperglycemic-
secretion (from pancreatic	n pancreatic	hyperosmolar coma,
 cells) by polypeptides of the	beptides of the	cardiovascular disease (e.g.,
invention (incl	invention (including antibodies	heart disease, atherosclerosis,
and agonists or	and agonists or antagonists of	microvascular disease,
the invention)	the invention) include assays	hypertension, stroke, and other
disclosed in: Shimizu, H., et	shimizu, H., et	diseases and disorders as
al., Endocr J, 47(3):261-9	47(3):261-9	described in the
(2000); Salapa	(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
Mol Endocrinc	Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
17 (1999); Fill	17 (1999); Filipsson, K., et al.,	endocrine disorders (as
Ann N Y Acad	Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
(1998); Olson,	(1998); Olson, L.K., et al., J	Disorders" section below),
Biol Chem, 27	Biol Chem, 271(28):16544-52	neuropathy, vision impairment
(1996); and, M	(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
Journal of Biomolecular	molecular	blindness), ulcers and impaired
Screening, 4:19	Screening, 4:193-204 (1999),	wound healing, and infection
the contents of	the contents of each of which	(e.g., infectious diseases and
is herein incorporated by	porated by	disorders as described in the
reference in its entirety.	s entirety.	"Infectious Diseases" section

				Pancreatic cells that may be used according to these assays	below, especially of the urinary tract and skin), carpal
				are publicly available (e.g.,	tunnel syndrome and
				through the ATCC) and/or	Dupuytren's contracture).
				may be routinely generated.	An additional highly preferred
				Exemplary pancreatic cells that	indication is obesity and/or
				may be used according to these	complications associated with
-				assays include HITT15 Cells.	obesity. Additional highly
				HITT15 are an adherent	preferred indications include
				epithelial cell line established	weight loss or alternatively,
				from Syrian hamster islet cells	weight gain. Additional highly
				transformed with SV40. These	preferred indications are
				cells express glucagon,	complications associated with
				somatostatin, and	insulin resistance.
				glucocorticoid receptors. The	
				cells secrete insulin, which is	
				stimulated by glucose and	
				glucagon and suppressed by	
				somatostatin or	
				glucocorticoids. ATTC# CRL-	
				1777 Refs: Lord and	
				Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
501	HSIDJ81	1449	TNFa in Human T-cell 2B9		
	HSIDJ81	1449	Activation of	Assays for the activation of	Preferred embodiments of the
501			transcription	transcription through the	invention include using
			through NFKB	NFKB response element are	polypeptides of the invention
			response element in	well-known in the art and may	(or antibodies, agonists, or

neuronal cells (such	be used or routinely modified	antagonists thereof) in
as Statistic Cells).	polypeptides of the invention	prevention, and/or treatment of
	(including antibodies and	Neurological Diseases and
	agonists or antagonists of the	Disorders (e.g. Alzheimer"s
	invention) to regulate NFKB	Disease, Parkinson"s Disease,
	transcription factors and	Brain Cancer, Seizures).
	modulate expression of	
	neuronal genes. Exemplary	
	assays for transcription	
	through the NFKB response	
	element that may be used or	
	routinely modified to test	
	NFKB-response element	
	activity of polypeptides of the	
	invention (including antibodies	
	and agonists or antagonists of	
	the invention) include assays	
	disclosed in: Gill JS, et al.,	
	Neurobiol Dis, 7(4):448-461	
	(2000); Tamatani M, et al., J	
	Biol Chem, 274(13):8531-	
	8538 (1999); Berger et al.,	
	Gene 66:1-10 (1998); Cullen	
	and Malm, Methods in	
	Enzymol 216:362-368 (1992);	
	Henthorn et al., Proc Natl	
	Acad Sci USA 85:6342-6346	
	(1988); Valle Blazquez et al,	
	Immunology 90(3):455-460	
	(1997); Aramburau et al., J	

	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkin's lymphoma, non-Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and uninary cancer. Other
Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety.  Neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary neuronal cells that may be used according to these assays include the SKNMC neuronal cell line.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription
	Activation of transcription through GAS response element in immune cells (such as T-cells).
	1450
	HSIDX71
	502

	element that may be used or	preferred indications include
	routinely modified to test	
	GAS-response element activity	
	of polypeptides of the	conditions, such as, for
	invention (including antibodies	s example, hyperplasia,
	and agonists or antagonists of	metaplasia, and/or dysplasia.
	the invention) include assays	Preferred indications include
	disclosed in Berger et al., Gene	
	66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
	Malm, Methods in Enzymol	lupus erythematosis, multiple
	216:362-368 (1992); Henthorn	sclerosis and/or as described
	et al., Proc Natl Acad Sci USA	below), immunodeficiencies
	85:6342-6346 (1988);	(e.g., as described below),
	Matikainen et al., Blood	boosting a T cell-mediated
	93(6):1980-1991 (1999); and	immune response, and
	Henttinen et al., J Immunol	suppressing a T cell-mediated
	155(10):4582-4587 (1995), the	
	contents of each of which are	preferred indications include
_	herein incorporated by	inflammation and
	reference in its entirety.	inflammatory disorders.
	Exemplary mouse T cells that	Highly preferred indications
	may be used according to these	
-	assays are publicly available	as described below under
	(e.g., through the ATCC).	"Immune Activity", "Blood-
	Exemplary T cells that may be	Related Disorders", and/or
	used according to these assays	"Cardiovascular Disorders"),
	include the CTLL cell line,	
	which is a suspension culture	infections, tuberculosis,
	of IL-2 dependent cytotoxic T	infections associated with
	cells.	chronic granulomatosus
		disease and malignant

osteoporosis, and/or an	infectious disease as described	ווויכיווסטט מוטכמט מוטכמט מיט מבטכווסכמ	Delow under Infectious	Disease"). An additional	preferred indication is	idionathic nulmonary fibrosis	Draferrad indications include	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease, and	asthma and allergy.	Kinase assay. Kinase assays,	IRK for example an Elk-1 kinase embodiment of the invention	athway assay, for ERK signal includes a method for	transduction that regulate cell stimulating adipocyte	proliferation or differentiation proliferation. An alternative	are well known in the art and highly preferred embodiment	may be used or routinely of the invention includes a
														-											HSJBQ79   1451	503   Adipocyte ERK	Signaling Pathway				

A =																	25	Š			er								
adipocyte proliferation. A highly preferred embodiment	of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation. A highly	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred
of polypeptides of the invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these
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indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as	described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders	(e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases").	and infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An	additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease	(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below).	diabetic neuropathy, nerve
assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays	include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed	through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art				

preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathics, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders. Throsis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, panereatic,	indication is obesity and/or complications associated with obesity. Additional highly
weignt gain. Additional highly preferred indications are complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, lung, pancreatic, lung, pancreatic,	preferred indications include weight loss or alternatively,
complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, acidisorders. Preferred indications include neoplasms and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	weight gain. Additional highly preferred indications are
Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders. Ibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	complications associated with insulin resistance
indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and brasst, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	Additional highly preferred
musculosketetal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	indications are disorders of the
muscular dystrophy, and/or as described herein.  Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, and kidney diseases or disorders. Throsis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	musculoskeletal systems
described herein.  Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	muscular dystrophy, and/or as
Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	described herein.
indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	Additional highly preferred
hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	indications include,
gallstones, osteoarthritis, degenerative arthritis, ating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	hypertension, coronary artery
ganstones, osteoartnrits, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	disease, dysnipidemia,
disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	gallstones, osteoarthritis,
and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	disorders, fibrosis, cachexia,
disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	and kidney diseases or
indications include neoplasms and cancer, such as, Iymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	disorders. Preferred
and cancer, such as, Iymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	indications include neoplasms
lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	and cancer, such as,
breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	lymphoma, leukemia and
cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic,	breast, colon, and kidney
indications include melanoma, prostate, lung, pancreatic,	cancer. Additional preferred
prostate, lung, pancreatic,	indications include melanoma,
	prostate, lung, pancreatic,

HSKCP69 1452 Activation of transcription through GATA response eleme immune cells (as mast cells).			esophageal, stomach, brain,
1452			liver, and urinary cancer.
1452			Highly preferred indications
1452			include lipomas and
1452			liposarcomas. Other preferred
1452			indications include benign
1452			dysproliferative disorders and
1452			pre-neoplastic conditions, such
1452			as, for example, hyperplasia,
1452			metaplasia, and/or dysplasia.
transcription through GATA response eleme immune cells ( as mast cells).		This reporter assay measures	Highly preferred indications
through GATA response eleme immune cells (as mast cells).		activation of the GATA-3	include allergy, asthma, and
response eleme immune cells (as mast cells).	through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
immune cells (as mast cells).	response element in	human mast cell line.	indications include infection
as mast cells).	immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
		cells has been linked to	described below under
		cytokine and chemokine	"Infectious Disease"), and
		production. Assays for the	inflammation and
		activation of transcription	inflammatory disorders.
		through the GATA3 response	Preferred indications also
		element are well-known in the	include blood disorders (e.g.,
		art and may be used or	as described below under
		routinely modified to assess	"Immune Activity", "Blood-
		the ability of polypeptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
		antibodies and agonists or	Preferred indications include
		antagonists of the invention) to	autoimmune diseases (e.g.,
		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
		expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and

development. Exemplary	immunodeficiencies (e.g., as
assays for transcription	described below). Preferred
through the GATA3 response	indications include neoplastic
element that may be used or	diseases (e.g., leukemia,
routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
activity of polypeptides of the	pancreatic, esophageal,
invention (including antibodies	stomach, brain, liver, and
and agonists or antagonists of	urinary tract cancers and/or as
the invention) include assays	described below under
disclosed in Berger et al., Gene	"Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
 et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);	Preferred indications include
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
contents of each of which are	lymphoma, arthritis, AIDS,
herein incorporated by	granulomatous disease,
reference in its entirety. Mast	inflammatory bowel disease,
cells that may be used	sepsis, neutropenia,
according to these assays are	neutrophilia, psoriasis,
publicly available (e.g.,	suppression of immune
through the ATCC).	reactions to transplanted

				Exemplary human mast cells that may be used according to these assays include the HMC-	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,
				1 cell line, which is an immature human mast cell line	meningitis, and Lyme Disease.
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HSKCP69	1452	Activation of	This reporter assay measures	Highly preferred indications
504			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
_			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
	-	*****		known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and

involved in	immunodeficiencies (e.g., as
immunomodulatory functions.	described below). Preferred
Exemplary assays for	indications include neoplastic
transcription through the	diseases (e.g., leukemia,
NFAT response element that	lymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
 (including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
 85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et al., J Immunol	leukemias, Hodgkin's disease,
165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
   16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
al., J Exp Med 188:527-537	granulomatous disease,
(1998), the contents of each of	inflammatory bowel disease,
which are herein incorporated	sepsis, neutropenia,
by reference in its entirety.	neutrophilia, psoriasis,
Mast cells that may be used	suppression of immune
according to these assays are	reactions to transplanted

				publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
505	HSKDA27	1453	MCP-1 in HUVEC		
505			CSF	expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes-macrophage progenitors and	embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a
				enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes	method for inhibiting the production of GM-CSF. Highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred
				and increases antigen presentation. GM-CSF is considered to be a proinflammatory cytokine.	indication is infection (e.g., as described below under "Infectious Disease". Highly preferred indications

		Assays for immunomodulatory	include blood disorders (e.g.,
		proteins that promote the	neutropenia (and the
		production of GM-CSF are	prevention of neutropenia
		well known in the art and may	(e.g., in HIV infected patients),
		be used or routinely modified	and/or as described below
-		to assess the ability of	under "Immune Activity",
		polypeptides of the invention	"Blood-Related Disorders",
		(including antibodies and	and/or "Cardiovascular
		agonists or antagonists of the	Disorders"). Highly preferred
		invention) to mediate	indications also include
		immunomodulation and	autoimmune diseases (e.g.,
		modulate the growth and	rheumatoid arthritis, systemic
		differentiation of leukocytes.	lupus erythematosis, multiple
		Exemplary assays that test for	sclerosis and/or as described
		immunomodulatory proteins	below) and
		evaluate the production of	immunodeficiencies (e.g., as
		cytokines, such as GM-CSF,	described below). Additional
		and the activation of T cells.	highly preferred indications
		Such assays that may be used	include asthma. Highly
		or routinely modified to test	preferred indications include
		immunomodulatory activity of	neoplastic diseases (e.g.,
		polypeptides of the invention	leukemia (e.g., acute
		(including antibodies and	lymphoblastic leukemia, and
		agonists or antagonists of the	acute myelogenous leukemia),
		invention) include the assays	lymphoma (e.g., non-
		disclosed in Miraglia et al., J	Hodgkin"s lymphoma and
		Biomolecular Screening 4:193-	Hodgkin"s disease), and/or as
		204 (1999); Rowland et al.,	described below under
		"Lymphocytes: a practical	"Hyperproliferative
		approach" Chapter 6:138-160	Disorders"). Highly preferred
		(2000); and Ye et al., J Leukoc	indications include neoplasms

	Biol (58(2):225-233, the	and cancers, such as, leukemia,
	contents of each of which are	lymphoma, melanoma, and
	herein incorporated by	prostate, breast, lung, colon,
	reference in its entirety.	pancreatic, esophageal,
	Natural killer cells that may be	stomach, brain, liver and
	used according to these assays	urinary cancer. Other preferred
	are publicly available (e.g.,	indications include benign
	through the ATCC) or may be	dysproliferative disorders and
	isolated using techniques	pre-neoplastic conditions, such
	disclosed herein or otherwise	as, for example, hyperplasia,
	known in the art. Natural	metaplasia, and/or dysplasia.
	killer (NK) cells are large	Highly preferred indications
	granular lymphocytes that have	include: suppression of
	cytotoxic activity but do bind	immune reactions to
	antigen. NK cells show	transplanted organs and tissues
	antibody-independent killing	(e.g., bone marrow transplant);
	of tumor cells and also	accelerating myeloid recovery;
	recognize antibody bound on	and mobilizing hematopoietic
 	target cells, via NK Fc	progenitor cells. Preferred
	receptors, leading to cell-	indications include boosting a
	mediated cytotoxicity.	T cell-mediated immune
		response, and alternatively,
		suppressing a T cell-mediated
		immune response. Preferred
		indications include anemia,
		pancytopenia, leukopenia,
_		thrombocytopenia, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous

505	HSKDA27	1453	Regulation of apoptosis in pancreatic beta cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergy.  A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease
2020				agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and progression of diabetes. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Loweth, AC, et al., FEBS Lett, 400(3):285-8 (1997); Saini, KS, et al.,	(e.g., renal tailure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g.,

	Biochem Mol Biol Int,	heart disease, atherosclerosis,
	39(6):1229-36 (1996);	microvascular disease,
	Krautheim, A., et al., Br J	hypertension, stroke, and other
	Pharmacol, 129(4):687-94	diseases and disorders as
	(2000); Chandra J, et al.,	described in the
	Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"
	(2001); Suk K, et al., J	section below), dyslipidemia,
	Immunol, 166(7):4481-9	endocrine disorders (as
	(2001); Tejedo J, et al., FEBS	described in the "Endocrine
	Lett, 459(2):238-43 (1999);	Disorders" section below),
	Zhang, S., et al., FEBS Lett,	neuropathy, vision impairment
	455(3):315-20 (1999); Lee et	(e.g., diabetic retinopathy and
	al., FEBS Lett 485(2-3): 122-	blindness), ulcers and impaired
	126 (2000); Nor et al., J Vasc	wound healing, and infection
	Res 37(3): 209-218 (2000);	(e.g., infectious diseases and
	and Karsan and Harlan, J	disorders as described in the
	Atheroscler Thromb 3(2): 75-	"Infectious Diseases" section
	80 (1996); the contents of each	below, especially of the
	of which are herein	urinary tract and skin), carpal
	incorporated by reference in its	tunnel syndrome and
	entirety. Pancreatic cells that	Dupuytren's contracture).
	may be used according to these	An additional highly preferred
	assays are publicly available	indication is obesity and/or
	(e.g., through the ATCC)	complications associated with
	and/or may be routinely	obesity. Additional highly
	generated. Exemplary	preferred indications include
	pancreatic cells that may be	weight loss or alternatively,
	used according to these assays	weight gain. Aditional
	include RIN-m. RIN-m is a	highly preferred indications are
	rat adherent pancreatic beta	complications associated with
	cell insulinoma cell line	insulin resistance.

				derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980	
505	HSKDA27	1453	Caspase (+paclitaxel) in SW480		
506	HSKHZ81	1454	SEAP in 293/ISRE		
	HSKH781	1454	Activation of	Assave for the activation of	A highly preferred indication
206			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
_			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other

3T3-L1/CRE reporter assay	diseases and disorders as
may be used to identify factors	described in the "Renal
that activate the cAMP	Disorders" section below),
signaling pathway. CREB	diabetic neuropathy, nerve
plays a major role in	disease and nerve damage
adipogenesis, and is involved	(e.g., due to diabetic
in differentiation into	neuropathy), blood vessel
adipocytes. CRE contains the	blockage, heart disease, stroke,
binding sequence for the	impotence (e.g., due to diabetic
transcription factor CREB	neuropathy or blood vessel
(CRE binding protein).	blockage), seizures, mental
 Exemplary assays for	confusion, drowsiness,
transcription through the	nonketotic hyperglycemic-
cAMP response element that	hyperosmolar coma,
may be used or routinely	cardiovascular disease (e.g.,
modified to test cAMP-	heart disease, atherosclerosis,
response element activity of	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in Berger et al., Gene	section below), dyslipidemia,
66:1-10 (1998); Cullen and	endocrine disorders (as
Malm, Methods in Enzymol	described in the "Endocrine
216:362-368 (1992); Henthorn	Disorders" section below),
et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
et al., Mol Cell Biol	blindness), ulcers and impaired
 20(3):1008-1020 (2000); and	wound healing, and infection
 Klemm et al., J Biol Chem	(e.g., infectious diseases and
273:917-923 (1998), the	disorders as described in the

				contents of each of which are herein incorporated by	"Infectious Diseases" section below, especially of the
				reference in its entirety. Pre-	urinary tract and skin), carpal
				adipocytes that may be used	tunnel syndrome and
				according to these assays are	Dupuytren's contracture).
				through the ATCC) and/or	indications are complications
				may be routinely generated.	associated with insulin
				Exemplary mouse adipocyte	resistance.
				cells that may be used	
				according to these assays	
				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
	HSKHZ81	1454	Inhibition of	Reporter Assay: construct	
909			squalene synthetase	contains regulatory and coding	
			gene transcription.	sequence of squalene	
				synthetase, the first specific	
				enzyme in the cholesterol	
				biosynthetic pathway. See	
				Jiang, et al., J. Biol. Chem.	
				268:12818-128241(993), the	
				contents of which are herein	
				incorporated by reference in its	

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its
	Production of ICAM-1
	1454
	HSKHZ81
	909

				used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be	
				include microvascular endothelial cells (MVEC).	
506	HSKHZ81	1454	Caspase (+paclitaxel) in SW480		
	HSKNB56	1455	Activation of	Kinase assay. Kinase assays,	A highly preferred
507			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for EKK signal	includes a method for stimulating adinocyte
				naissuction of differentiation	sunnuating ampocyte proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
				inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
-				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
				test ERK kinase-induced	differentiation. A highly
				activity of polypeptides of the	preferred embodiment of the

	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
	the invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
-	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
-	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
	according to these assays	stroke, impotence and/or as
	include 3T3-L1 cells. 3T3-L1	described below under
	is an adherent mouse	"Immune Activity",
	preadipocyte cell line that is a	"Cardiovascular Disorders",
	continuous substrain of 3T3	and/or "Blood-Related
	fibroblast cells developed	Disorders"), immune disorders
	through clonal isolation and	(e.g., as described below under

ocyte to "Immune Activity"), neural rision under disorders (e.g., as described hitation below under "Neural Activity and Neurological Diseases.").	 A highly preferred indication is diabetes mellitus.	additional highly preferred	indication is a complication associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,
adipose-like conversion under appropriate differentiation conditions known in the art																						
			_																			

					musculoskeletal systems
					including myopathies.
					muscular dystrophy, and/or as
					described herein.
					Additional highly preferred
					indications include,
-					hypertension, coronary artery
					disease, dyslipidemia,
					gallstones, osteoarthritis,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
					indications include neoplasms
					and cancer, such as,
					lymphoma, leukemia and
					breast, colon, and kidney
					cancer. Additional preferred
					indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
TSH	CQ82	1456	Activation of	Assays for the activation of	A preferred embodiment of

the invention includes a	method for inhibiting (e.g.,	reducing) TNF alpha	production. An alternative	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in
transcription through the	Serum Response Element	(SRE) are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by
transcription	through serum	response element in	immune cells (such	as T-cells).													_													
208							_										_													

patients with rheumatoid arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple
reference in its entirety. T cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.																			
																	-												

myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes-macrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes, and increases artises.
	Production of GM-CSF
	1457
	HSLJG37
	509

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-	nder	e".	ndication	rders (e.§	he	ropenia	ted patie	d below	ctivity",	isorders"	cular	y preferr	clude	ses (e.g.,	is, systen	is, multip	describe		es (e.g., a	Addition	dications	Highly	ns includ	s (e.g.,	ıte	cemia, an	s leukem	-uo	ma and	) J/
-	pelow n	s Diseas	eferred in	ood diso	ia (and t	1 of neut	IV infec	describe	mune A	elated Di	ardiovas	"). Highl	s also in	ne disea	d arthriti	hematos	ind/or as	þ	eficiencia	below).	ferred in	thma.	indicatio	diseases	(e.g., act	astic leuk	logenous	a (e.g., n	s lymphc	diam's
:	described below under	"Infectious Disease"	Highly preferred indications	include blood disorders (e.g.,	neutropenia (and the	prevention of neutropenia	(e.g., in HIV infected patients),	and/or as described below	under "Immune Activity",	"Blood-Related Disorders",	and/or "Cardiovascular	Disorders"). Highly preferred	indications also include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include asthma. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia (e.g., acute	lymphoblastic leukemia, and	acute myelogenous leukemia),	lymphoma (e.g., non-	Hodgkin"s lymphoma and	11. Jal. 11. 11. 11. 11. 11. 11.
	18		ne.	ulatory	<u> </u>	are	d may	diffed	-	ntion	p	f the		•	_	ytes.	est for	teins	of	CSF,	ells.	pesn	test		tion	-		ssays	al., J	_
100	presentation. GM-CSF is	e a	proinflammatory cytokine.	Assays for immunomodulatory	proteins that promote the	production of GM-CSF are	well known in the art and may	be used or routinely modified	ility of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	ediate	immunomodulation and	modulate the growth and	differentiation of leukocytes.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as GM-CSF,	and the activation of T cells.	Such assays that may be used	or routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	
.,	tation.	considered to be a	lammato	s for imn	ns that pr	ction of (	nown in	d or rout	to assess the ability of	eptides of	ding antil	ts or anta	invention) to mediate	nomodula	ate the g	ntiation	olary assa	npomou	te the pro	nes, such	e activati	issays tha	inely mo	nomodula	ptides of	ling antil	ts or anta	ion) inch	sed in Mi	Diamatanta (G. 10)
	presen	consid	proinf	Assay	protein	produc	well k	be use	to asse	polype	(inclue	agonis	invent	immui	modu	differe	Exem	immui	evalua	cytoki	and th	Such a	or rout	immul	polype	(inclue	agonis	invent	disclos	District
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	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); and Ye et al., J Leukoc	indications include neoplasms
	Biol (58(2):225-233, the	and cancers, such as, leukemia,
	contents of each of which are	lymphoma, melanoma, and
	herein incorporated by	prostate, breast, lung, colon,
	reference in its entirety.	pancreatic, esophageal,
	Natural killer cells that may be	stomach, brain, liver and
	used according to these assays	urinary cancer. Other preferred
	are publicly available (e.g.,	indications include benign
	through the ATCC) or may be	dysproliferative disorders and
	isolated using techniques	pre-neoplastic conditions, such
	disclosed herein or otherwise	as, for example, hyperplasia,
	known in the art. Natural	metaplasia, and/or dysplasia.
	killer (NK) cells are large	Highly preferred indications
	granular lymphocytes that have	include: suppression of
	cytotoxic activity but do bind	immune reactions to
	antigen. NK cells show	transplanted organs and tissues
	antibody-independent killing	(e.g., bone marrow transplant);
	of tumor cells and also	accelerating myeloid recovery;
	recognize antibody bound on	and mobilizing hematopoietic
	target cells, via NK Fc	progenitor cells. Preferred
	receptors, leading to cell-	indications include boosting a
	mediated cytotoxicity.	T cell-mediated immune
		response, and alternatively,
		suppressing a T cell-mediated
		immune response. Preferred
		indications include anemia,
		pancytopenia, leukopenia,
		thrombocytopenia, acute
		lymphocytic anemia (ALL),

plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergy.	
	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the Cell Titer-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1458
	HSODE04
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	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infantions are productions.
presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits lgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be
	Production of IFNgamma using a T cells
	1458
	HSODE04
	510

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assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (including Corcening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin	assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulatior, regulate imflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160

				Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
				Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
				et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
				15:749-795 (1997), and	esophageal, stomach, brain,
				Rheumatology (Oxford)	liver and urinary cancer. Other
				38(3):214-20 (1999), the	preferred indications include
				contents of each of which are	benign dysproliferative
				herein incorporated by	disorders and pre-neoplastic
				reference in its entirety.	conditions, such as, for
				Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
-					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
510	HSODE04	1458	IFNg in Human T- cell 2B9		

	HSPBF70	1459	CD152 in Human T		
511			cells		
	HSQEO84	1460	Regulation of	Assays for the regulation (i.e.	Highly preferred indications
512			viability or	increases or decreases) of	include eosinophilia, asthma,
			proliferation of	viability and proliferation of	allergy, hypersensitivity
			immune cells (such	cells in vitro are well-known in	reactions, inflammation, and
			as human	the art and may be used or	inflammatory disorders.
			eosinophil EOL-1	routinely modified to assess	Additional highly preferred
			cells).	the ability of polypeptides of	indications include immune
				the invention (including	and hematopoietic disorders
				antibodies and agonists or	(e.g., as described below under
				antagonists of the invention) to	"Immune Activity", and
				regulate viability and	"Blood-Related Disorders"),
				proliferation of eosinophil cells	autoimmune diseases (e.g.,
				and cell lines. For example,	rheumatoid arthritis, systemic
				the CellTiter-Gloô	lupus erythematosis, Crohn"s
				Luminescent Cell Viability	disease, multiple sclerosis
				Assay (Promega Corp.,	and/or as described below),
				Madison, WI, USA) can be	immunodeficiencies (e.g., as
				used to measure the number of	described below). Highly
				viable cells in culture based on	preferred indications also
				quantitation of the ATP	include boosting or inhibiting
				present which signals the	immune cell proliferation.
				presence of metabolically	Preferred indications include
				active cells. Eosinophils are a	neoplastic diseases (e.g.,
				type of immune cell important	leukemia, lymphoma, and/or as
				in allergic responses; they are	described below under
	-			recruited to tissues and	"Hyperproliferative
				mediate the inflammtory	Disorders"). Highly preferred
				response of late stage allergic	indications include boosting an
				reaction. Eosinophil cell lines	eosinophil-mediated immune

				that may be used according to these assays are publicly available and/or may be routinely generated.  Exemplary eosinophil cells that may be used according to these assays include EOL-1 Cells.	response, and suppressing an eosinophil-mediated immune response.
512	HSQE084	1460	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
				development. Exemplary assays for transcription	immunodeficiencies (e.g., as described below). Preferred

cemia,	oma,	ng, colon,	geal,	ver, and	rs and/or as	nder	e	r preferred	e benign	sorders and	ditions, such	yperplasia,	dysplasia.	ons include	enia,	bocytopenia,	in's disease,	anemia	omas,	, Burkitt's	is, AIDS,	ease,	el disease,	a,	asis,	mune	lanted	, hemophilia,	
diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	
Inrougn the GATAS response element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	
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ditis,	indication sthma, and all preferr le infectio les disease aunder se"), and le ons also orders (e.g. w under y", "Blooc s", and/or Disorders' ons incluctus ases (e.g., tis, system sis, multip s describe	ies (e.g., a
meningitis, and Lyme Disease.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Preferred
mellitu mening	Highly prefinclude allerhinitis. Ac indications (e.g., an inf described by "Infectious inflammation inflammation preferred ir include bloo as described "Immune A Related Dis "Cardiovass Preferred ir autoimmun rheumatoid lupus eryth sclerosis an below) and	immur
these assays include the HMC-  1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line.  Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes	involved in immunomodulatory functions.
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	Activation of transcription through NFAT response element in immune cells (such as mast cells).	
	1460	
	HSQE084	
	512	

	Exemplary assays for	indications include neoplastic
	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
	 response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	 31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
-	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
	which are herein incorporated	sepsis, neutropenia,
	 by reference in its entirety.	neutrophilia, psoriasis,
	 Mast cells that may be used	suppression of immune
	according to these assays are	reactions to transplanted
	publicly available (e.g.,	organs and tissues, hemophilia,
	through the ATCC).	hypercoagulation, diabetes

				Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of	meningitis, and Lyme Disease.
512	HSQE084	1460	Proliferation of preadipose cells (such as 3T3-L1 cells)	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the Cell Titer-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on	
				quantitation of the ATP present which signals the	

			presence of metabolically active cells. 3T3-L1 is a	
			mouse preadipocyte cell line. It is a continuous substrain of	
			3T3 fibroblast cells developed	
			through clonal isolation. Cells	
			were differentiated to an	
			adipose-like state before being	
			used in the screen. See Green	
			H and Meuth M., Cell 3: 127-	
			133 (1974), which is herein	
			incorporated by reference in its	
			entirety.	
HSQE084	1460	Production of	Endothelial cells, which are	Highly preferred indications
		ICAM in	cells that line blood vessels,	include inflammation (acute
		endothelial cells	and are involved in functions	and chronic), restnosis,
		such as human	that include, but are not limited	atherosclerosis, asthma and
		umbilical vein	to, angiogenesis, vascular	allergy. Highly preferred
		endothelial cells	permeability, vascular tone,	indications include
 		(HUVEC))	and immune cell extravasation.	inflammation and
			Exemplary endothelial cells	inflammatory disorders,
			that may be used in ICAM	immunological disorders,
			production assays include	neoplastic disorders (e.g.
			human umbilical vein	cancer/tumorigenesis), and
			endothelial cells (HUVEC),	cardiovascular disorders (such
			and are available from	as described below under
			commercial sources. The	"Immune Activity", "Blood-
			expression of ICAM (CD54),a	Related Disorders",
			intergral membrane protein,	"Hyperproliferative Disorders"
			can be upregulated by	and/or "Cardiovascular
			cytokines or other factors, and	Disorders"). Highly preferred

				1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( )
		-		In mediating immune and	and cancers such as, for
				endothelial cell interactions	example, leukemia, lymphoma,
				leading to immune and	melanoma, renal cell
				inflammatory responses.	carcinoma, and prostate,
				Assays for measuring	breast, lung, colon, pancreatic,
				expression of ICAM-1 are	esophageal, stomach, brain,
				well-known in the art and may	liver and urinary cancer. Other
				be used or routinely modified	preferred indications include
				to assess the ability of	benign dysproliferative
				polypeptides of the invention	disorders and pre-neoplastic
				(including antibodies and	conditions, such as, for
				agonists or antagonists of the	example, hyperplasia,
				invention) to regulate ICAM-1	metaplasia, and/or dysplasia.
				expression. Exemplary assays	
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Rolfe BE, et al.,	
				Atherosclerosis, 149(1):99-110	
				(2000); Panettieri RA Jr, et al.,	
				J Immunol, 154(5):2358-2365	
				(1995); and, Grunstein MM, et	
				al., Am J Physiol Lung Cell	
				Mol Physiol, 278(6):L1154-	
				L1163 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety.	
512	HSQEO84	1460	IL-6 in HUVEC		

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RANTES FMAT. Assays for	immunomodulatory proteins	that induce chemotaxis of T	cells, monocytes, and	eosinophils are well known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	induce chemotaxis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-
Production of	RANTES in	endothelial cells	(such as human	umbilical vein	endothelial cells	(HUVEC))																								
1460							~							-																
HSQE084		_													_															
	512														20															

	09	100	(5);	dx	l of	ted		pe	ays			S	to		cells			are		to,			tion.		vell-   include inflammation (acute	e and chronic), restnosis,	to atherosclerosis, asthma and	ollower Iliable and found
204 (1999); Rowland et al., "Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	2/0(5243):1811-1815 (1995); and Dobinson of al. Clin Evn.	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.	Assays for measuring	expression of VCAM are well-	known in the art and may be	used or routinely modified to	access the ability of
															-									Production of	VCAM in	endothelial cells	(such as human	umbilical vein
																								1460				
																								HSQEO84				
				·														,							512			

endothelial cells	polypeptides of the invention	indications include
 (HUVEC))	(including antibodies and	inflammation and
	agonists or antagonists of the	inflammatory disorders,
	invention) to regulate VCAM	immunological disorders,
	expression. For example,	neoplastic disorders (e.g.
	FMAT may be used to meaure	cancer/tumorigenesis), and
	the upregulation of cell surface	cardiovascular disorders (such
	VCAM-1 expresssion in	as described below under
	endothelial cells. Endothelial	"Immune Activity", "Blood-
-	cells are cells that line blood	Related Disorders",
	vessels, and are involved in	"Hyperproliferative Disorders"
	functions that include, but are	and/or "Cardiovascular
	not limited to, angiogenesis,	Disorders"). Highly preferred
	vascular permeability, vascular	indications include neoplasms
	tone, and immune cell	and cancers such as, for
	extravasation. Exemplary	example, leukemia, lymphoma,
	endothelial cells that may be	melanoma, renal cell
	used according to these assays	carcinoma, and prostate,
	include human umbilical vein	breast, lung, colon, pancreatic,
	endothelial cells (HUVEC),	esophageal, stomach, brain,
	which are available from	liver and urinary cancer. Other
	commercial sources. The	preferred indications include
	expression of VCAM	benign dysproliferative
	(CD106), a membrane-	disorders and pre-neoplastic
	associated protein, can be	conditions, such as, for
	upregulated by cytokines or	example, hyperplasia,
	other factors, and contributes	metaplasia, and/or dysplasia.
	to the extravasation of	
	lymphocytes, leucocytes and	
	other immune cells from blood	
	vessels; thus VCAM	

				expression plays a role in promoting immune and inflammatory responses.	
512	HSQEO84	1460	SEAP in Senescence Assay		
	HSSAJ29	1461	Activation of	Assays for the activation of	Preferred indications
513			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are known in	(e.g., as described below under
			response element in	the art and may be used or	"Hyperproliferative
			immune cells (such	routinely modified to assess	Disorders"), blood disorders
			as T-cells).	the ability of polypeptides of	(e.g., as described below under
				the invention (including	"Immune Activity",
				antibodies and agonists or	"Cardiovascular Disorders",
				antagonists of the invention) to	and/or "Blood-Related
				modulate growth and other cell	Disorders"), and infection
				functions. Exemplary assays	(e.g., an infectious disease as
				for transcription through the	described below under
				AP1 response element that	"Infectious Disease"). Highly
				may be used or routinely	preferred indications include
				modified to test AP1-response	autoimmune diseases (e.g.,
				element activity of	rheumatoid arthritis, systemic
				polypeptides of the invention	lupus erythematosis, multiple
				(including antibodies and	sclerosis and/or as described
				agonists or antagonists of the	below) and
				invention) include assays	immunodeficiencies (e.g., as
				disclosed in Berger et al., Gene	described below). Additional
				66:1-10 (1988); Cullen and	highly preferred indications
				Malm, Methods in Enzymol	include inflammation and
				216:362-368 (1992); Henthorn	inflammatory disorders.
				et al., Proc Natl Acad Sci USA	Highly preferred indications
				85:6342-6346 (1988);	also include neoplastic

					meningitis, and Lyme Disease.
	HSSDX51	1462	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
514				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
_				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
	=			proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
				agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and
				immunomodulation and	immunodeficiencies (e.g., as
				differentiation and modulate T	described below). Highly
				cell proliferation and function.	preferred indications also

Exemplary assays that test for	include boosting a B cell-
immunomodulatory proteins	mediated immune response
evaluate the production of	and alternatively suppressing a
cytokines, such as IL-6, and	B cell-mediated immune
the stimulation and	response. Highly preferred
upregulation of T cell	indications include
proliferation and functional	inflammation and
activities. Such assays that	inflammatory
may be used or routinely	disorders.Additional highly
modified to test	preferred indications include
immunomodulatory and	asthma and allergy. Highly
diffferentiation activity of	preferred indications include
polypeptides of the invention	neoplastic diseases (e.g.,
(including antibodies and	myeloma, plasmacytoma,
agonists or antagonists of the	leukemia, lymphoma,
invention) include assays	melanoma, and/or as described
disclosed in Miraglia et al., J	below under
Biomolecular Screening 4:193-	"Hyperproliferative
204(1999); Rowland et al.,	Disorders"). Highly preferred
"Lymphocytes: a practical	indications include neoplasms
approach" Chapter 6:138-160	and cancers, such as, myeloma,
(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
Immunol 158:2919-2925	lymphoma, melanoma, and
(1997), the contents of each of	prostate, breast, lung, colon,
which are herein incorporated	pancreatic, esophageal,
by reference in its entirety.	stomach, brain, liver and
Human dendritic cells that may	urinary cancer. Other preferred
be used according to these	indications include benign
assays may be isolated using	dysproliferative disorders and
techniques disclosed herein or	pre-neoplastic conditions, such
otherwise known in the art.	as, for example, hyperplasia,

				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HSSFT08	1463	Activation of	Assays for the activation of	A preferred embodiment of
515			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,

antibodies and agonists or	increasino) TNF alpha
antagonists of the invention) to	production Preferred
annagonists of the invention) to	
regulate the serum response	indications include blood
factors and modulate the	disorders (e.g., as described
expression of genes involved	below under "Immune
in growth. Exemplary assays	Activity", "Blood-Related
for transcription through the	Disorders", and/or
SRE that may be used or	"Cardiovascular Disorders"),
routinely modified to test SRE	Highly preferred indications
activity of the polypeptides of	include autoimmune diseases
the invention (including	(e.g., rheumatoid arthritis,
antibodies and agonists or	systemic lupus erythematosis,
antagonists of the invention)	Crohn"s disease, multiple
include assays disclosed in	sclerosis and/or as described
Berger et al., Gene 66:1-10	below), immunodeficiencies
(1998); Cullen and Malm,	(e.g., as described below),
Methods in Enzymol 216:362-	boosting a T cell-mediated
368 (1992); Henthorn et al.,	immune response, and
Proc Natl Acad Sci USA	suppressing a T cell-mediated
85:6342-6346 (1988); and	immune response. Additional
Black et al., Virus Genes	highly preferred indications
12(2):105-117 (1997), the	include inflammation and
content of each of which are	inflammatory disorders, and
herein incorporated by	treating joint damage in
reference in its entirety. T	patients with rheumatoid
cells that may be used	arthritis. An additional highly
according to these assays are	preferred indication is sepsis.
publicly available (e.g.,	Highly preferred indications
through the ATCC).	include neoplastic diseases
Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
may be used according to these	and/or as described below

8	assavs include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,
	dependent suspension culture	highly preferred indications
0	of T cells with cytotoxic	include neoplasms and
8	activity.	cancers, such as, for example,
		leukemia, lymphoma,
		melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted

		-	
		development. Exemplary	immunodeficiencies (e.g., as
-	-	assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
 -		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
•		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
		Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
		Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
		14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
-		contents of each of which are	lymphoma, arthritis, AIDS,
		herein incorporated by	granulomatous disease,
		reference in its entirety. Mast	inflammatory bowel disease,
		cells that may be used	sepsis, neutropenia,
		according to these assays are	neutrophilia, psoriasis,
		publicly available (e.g.,	suppression of immune
		through the ATCC).	reactions to transplanted

Nui	involved in	immunodeficiencies (e.g., as
umi	immunomodulatory functions.	described below). Preferred
Exe	Exemplary assays for	indications include neoplastic
tran	transcription through the	diseases (e.g., leukemia,
NE.	NFAT response element that	lymphoma, melanoma,
may	may be used or routinely	prostate, breast, lung, colon,
oom   moc	modified to test NFAT-	pancreatic, esophageal,
Isal	response element activity of	stomach, brain, liver, and
l pol	polypeptides of the invention	urinary tract cancers and/or as
(inc	(including antibodies and	described below under
ago	agonists or antagonists of the	"Hyperproliferative
hyni	invention) include assays	Disorders"). Other preferred
disc	disclosed in Berger et al., Gene	indications include benign
(99)	66:1-10 (1998); Cullen and	dysproliferative disorders and
Mai	Malm, Methods in Enzymol	pre-neoplastic conditions, such
216	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
eta	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6	85:6342-6346 (1988); De Boer	Preferred indications include
eta	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et a	et al., J Immunol	leukemias, Hodgkin's disease,
165	165(12):7215-7223 (2000);	acute lymphocytic anemia
Hut	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Bio	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
163	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
al.,	al., J Exp Med 188:527-537	granulomatous disease,
(196	(1998), the contents of each of	inflammatory bowel disease,
whi	which are herein incorporated	sepsis, neutropenia,
by r	by reference in its entirety.	neutrophilia, psoriasis,
Mas	Mast cells that may be used	suppression of immune
acc	according to these assays are	reactions to transplanted

_				publicly available (e.g., through the ATCC).	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
HSSGD52	7	1464	Proliferation of pre-	Assays for the regulation (i.e.	
			adipose cells (such	increases or decreases) of	
		-	as 3T3-L1 cells)	viability and proliferation of	
				cells in vitro are well-known in	
				the art and may be used or	
	-			routinely modified to assess	
				the ability of polypeptides of	
				the invention (including	
				antibodies and agonists or	
				antagonists of the invention) to	
				regulate viability and	
				proliferation of pre-adipose	
				cells and cell lines. For	
				example, the CellTiter-Gloô	
				Luminescent Cell Viability	
				Assay (Promega Corp.,	
				Madison, WI, USA) can be	
				used to measure the number of	
				viable cells in culture based on	

		A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related
quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.		Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the
	IL-2 in Human T-cell 293T	Activation of transcription through serum response element in immune cells (such as natural killer cells).
	1464	1464
	HSSGD52	HSSGD52
	516	516

4	function of growth-related	Disorders", and/or
 5.0	genes in many cell types.	"Cardiovascular Disorders"),
<u> </u>	Exemplary assays for	Highly preferred indications
t	transcription through the SRE	include autoimmune diseases
#	that may be used or routinely	(e.g., rheumatoid arthritis,
u	modified to test SRE activity	systemic lupus erythematosis,
0	of the polypeptides of the	Crohn"s disease, multiple
ii	invention (including antibodies	sclerosis and/or as described
a	and agonists or antagonists of	below), immunodeficiencies
1	the invention) include assays	(e.g., as described below),
P	disclosed in Berger et al., Gene	boosting a T cell-mediated
9	66:1-10 (1998); Cullen and	immune response, and
	Malm, Methods in Enzymol	suppressing a T cell-mediated
2	216:362-368 (1992); Henthorn	immune response. Additional
0	et al., Proc Natl Acad Sci USA	highly preferred indications
8	85:6342-6346 (1988); Benson	include inflammation and
ō	et al., J Immunol 153(9):3862-	inflammatory disorders, and
8	3873 (1994); and Black et al.,	treating joint damage in
	Virus Genes 12(2):105-117	patients with rheumatoid
	(1997), the content of each of	arthritis. An additional highly
 8	which are herein incorporated	preferred indication is sepsis.
4	by reference in its entirety. T	Highly preferred indications
3	cells that may be used	include neoplastic diseases
a	according to these assays are	(e.g., leukemia, lymphoma,
d	publicly available (e.g.,	and/or as described below
11	through the ATCC).	under "Hyperproliferative
Ш	Exemplary T cells that may be	Disorders"). Additionally,
n	used according to these assays	highly preferred indications
 ·i	include the NK-YT cell line,	include neoplasms and
8	which is a human natural killer	cancers, such as, for example,
5	cell line with cytolytic and	leukemia, lymphoma,

		cytotoxic activity.	melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
	_		conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
-			disease, inflammatory bowel
			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues, hemophilia,
			hypercoagulation, diabetes
			mellitus, endocarditis,
			meningitis, Lyme Disease,
			cardiac reperfusion injury, and
			asthma and allergy. An

					additional preferred indication
					disease as described below
					under "Infectious Disease").
	HSSGD52	1464	Activation of	Assays for the activation of	A highly preferred
516			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
			response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
			as T-cells).	well-known in the art and may	indications include
				be used or routinely modified	inflammation and
				to assess the ability of	inflammatory disorders.
				polypeptides of the invention	Preferred indications include
				(including antibodies and	blood disorders (e.g., as
				agonists or antagonists of the	described below under
				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
				modulate the expression of	"Cardiovascular Disorders").
				multiple genes. Exemplary	Preferred indications include
				assays for transcription	autoimmune diseases (e.g.,
				through the STAT6 response	rheumatoid arthritis, systemic
				element that may be used or	lupus erythematosis, multiple
				routinely modified to test	sclerosis and/or as described
				STAT6 response element	below) and
				activity of the polypeptides of	immunodeficiencies (e.g., as
				the invention (including	described below).
				antibodies and agonists or	Preferred indications include
				antagonists of the invention)	neoplastic diseases (e.g.,
				include assays disclosed in	leukemia, lymphoma,
				Berger et al., Gene 66:1-10	melanoma, and/or as described
				(1998); Cullen and Malm,	below under

		Methods in Enzymol 216:362-	"Hyperproliferative
		368 (1992); Henthorn et al.,	Disorders"). Preferred
		Proc Natl Acad Sci USA	indications include neoplasms
		85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
		et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
		(1998); Moffatt et al.,	prostate, breast, lung, colon,
-		Transplantation 69(7):1521-	pancreatic, esophageal,
		1523 (2000); Curiel et al., Eur	stomach, brain, liver and
		J Immunol 27(8):1982-1987	urinary cancer. Other preferred
		(1997); and Masuda et al., J	indications include benign
		Biol Chem 275(38):29331-	dysproliferative disorders and
		29337 (2000), the contents of	pre-neoplastic conditions, such
		each of which are herein	as, for example, hyperplasia,
		incorporated by reference in its	metaplasia, and/or dysplasia.
		entirety. T cells that may be	Preferred indications include
		used according to these assays	anemia, pancytopenia,
		are publicly available (e.g.,	leukopenia, thrombocytopenia,
		through the ATCC).	Hodgkin's disease, acute
		Exemplary T cells that may be	lymphocytic anemia (ALL),
		used according to these assays	plasmacytomas, multiple
		include the SUPT cell line,	myeloma, Burkitt's lymphoma,
		which is a suspension culture	arthritis, AIDS, granulomatous
		of IL-2 and IL-4 responsive T	disease, inflammatory bowel
	-	cells.	disease, sepsis, neutropenia,
_			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,
			meningitis, and Lyme Disease.

					An additional preferred indication is infection (e.g. an
					infectious disease as described
					below under "Infectious
	1				Disease").
	HSSGG82	1465	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
517			Apoptosis	caspase apoptosis are well	embodiment of the invention
				known in the art and may be	includes a method for
-				used or routinely modified to	stimulating endothelial cell
		_		assess the ability of	growth. An alternative highly
				polypeptides of the invention	preferred embodiment of the
				(including antibodies and	invention includes a method
,	~~~~~			agonists or antagonists of the	for inhibiting endothelial cell
				invention) to promote caspase	growth. A highly preferred
				protease-mediated apoptosis.	embodiment of the invention
				Induction of apoptosis in	includes a method for
				endothelial cells supporting the	stimulating endothelial cell
				vasculature of tumors is	proliferation. An alternative
				associated with tumor	highly preferred embodiment
				regression due to loss of tumor	of the invention includes a
				blood supply. Exemplary	method for inhibiting
				assays for caspase apoptosis	endothelial cell proliferation.
				that may be used or routinely	A highly preferred
				modified to test capase	embodiment of the invention
				apoptosis activity of	includes a method for
				polypeptides of the invention	stimulating apoptosis of
				(including antibodies and	endothelial cells. An
				agonists or antagonists of the	alternative highly preferred
				invention) include the assays	embodiment of the invention
				disclosed in Lee et al., FEBS	includes a method for
				Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)

	Nor et al TVasc Res 37(3).	anontosis of endothelial cells
	209-218 (2000); and Karsan	A highly preferred
	and Harlan, J Atheroscler	embodiment of the invention
	Thromb 3(2): 75-80 (1996);	includes a method for
	the contents of each of which	stimulating angiogenisis. An
	are herein incorporated by	alternative highly preferred
	reference in its entirety.	embodiment of the invention
	Endothelial cells that may be	includes a method for
	used according to these assays	inhibiting angiogenesis. A
	are publicly available (e.g.,	highly preferred embodiment
	through commercial sources).	of the invention includes a
	Exemplary endothelial cells	method for reducing cardiac
	that may be used according to	hypertrophy. An alternative
	these assays include bovine	highly preferred embodiment
	aortic endothelial cells	of the invention includes a
	(bAEC), which are an example	method for inducing cardiac
	of endothelial cells which line	hypertrophy. Highly
	blood vessels and are involved	preferred indications include
	in functions that include, but	neoplastic diseases (e.g., as
	are not limited to,	described below under
	angiogenesis, vascular	"Hyperproliferative
	permeability, vascular tone,	Disorders"), and disorders of
	and immune cell extravasation.	the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
·		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular
		disease, diabetic nephropathy,

intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	
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																					-									_

cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and
															-		_											-		

lymphedema; and other
vascular disorders such as
peripheral vascular disease,
and cancer. Highly
preferred indications also
include trauma such as
wounds, burns, and injured
 tissue (e.g., vascular injury
such as, injury resulting from
balloon angioplasty, and
atheroschlerotic lesions),
implant fixation, scarring,
ischemia reperfusion injury,
rheumatoid arthritis,
cerebrovascular disease, renal
diseases such as acute renal
failure, and osteoporosis.
Additional highly preferred
indications include stroke,
graft rejection, diabetic or
other retinopathies, thrombotic
and coagulative disorders,
vascularitis, lymph
angiogenesis, sexual disorders,
age-related macular
degeneration, and treatment
/prevention of endometriosis
and related conditions.
Additional highly preferred
indications include fibromas,
heart disease, cardiac arrest,

Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood- Related Disorders", and/or "Cardiovascular Disorders", and/or Preferred indications include autoimmune diseases (e.g., rheumatoria arthitis, systemic lupus expthematosis, multiple selerosis and/or as described below) and dirional preferred indications include immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammator					heart valve disease, and
1466 Regulation of Caspase Apoptosis. Assays for apoptosis of ammune cells (such as mast cells).  Sassess the ability of polypeptides of the invention (including antibodies and					vascular disease.
1466 Regulation of Caspase Apoptosis. Assays for apoptosis of ammune cells (such assess the ability of polypeptides of the invention (including antibodies and					Preferred indications include
1466 Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such as mast cells).  Begulation of caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and					blood disorders (e.g., as
1466 Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such as mast cells).  Begulation of caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and					described below under
1466 Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such as mast cells).  Begulation of caspase Apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and					"Immune Activity", "Blood-
Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such known in the art and may be as mast cells).  Samuel Caspase Apoptosis. Assays for caspase apoptosis are well immune cells (such known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and					Related Disorders", and/or
Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such as mast cells).  Sassess the ability of polypeptides of the invention (including antibodies and					"Cardiovascular Disorders").
Regulation of Caspase Apoptosis. Assays for apoptosis of immune cells (such as mast cells).  Sassess the ability of polypeptides of the invention (including antibodies and					Preferred indications include
Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such known in the art and may be as mast cells).  assess the ability of polypeptides of the invention (including antibodies and					autoimmune diseases (e.g.,
1466 Regulation of Caspase Apoptosis. Assays for apoptosis of immune cells (such as mast cells).  assess the ability of polypeptides of the invention (including antibodies and					rheumatoid arthritis, systemic
Regulation of Caspase Apoptosis. Assays for apoptosis of immune cells (such as mast cells).  as mast cells).  polypeptides of the invention (including antibodies and					lupus erythematosis, multiple
Regulation of Caspase Apoptosis. Assays for apoptosis of immune cells (such as mast cells).  as mast cells).  assess the ability of polypeptides of the invention (including antibodies and					sclerosis and/or as described
Regulation of Caspase Apoptosis. Assays for apoptosis of immune cells (such immune cells).  as mast cells).  ssess the ability of polypeptides of the invention (including antibodies and					below) and
Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such assass the ability of polypeptides of the invention (including antibodies and					immunodeficiencies (e.g., as
1466 Regulation of Caspase Apoptosis. Assays for apoptosis of immune cells (such as mast cells).  as mast cells).  polypeptides of the invention (including antibodies and					described below). Additional
1466 Regulation of Caspase Apoptosis. Assays for apoptosis of immune cells (such as mast cells).  as mast cells).  assess the ability of polypeptides of the invention (including antibodies and					preferred indications include
Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such as mast cells).  as mast cells).  assess the ability of polypeptides of the invention (including antibodies and					inflammation and
Regulation of Caspase Apoptosis. Assays for apoptosis of immune cells (such as mast cells).  as mast cells).  assess the ability of polypeptides of the invention (including antibodies and					inflammatory disorders (such
Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such as mast cells).  as mast cells).  polypeptides of the invention (including antibodies and					as acute and chronic
Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such as mast cells).  as mast cells).  assess the ability of polypeptides of the invention (including antibodies and					inflammatory diseases, e.g.,
Regulation of Caspase Apoptosis. Assays for apoptosis of immune cells (such as mast cells).  as mast cells).  assess the ability of polypeptides of the invention (including antibodies and					inflammatory bowel disease
Regulation of Caspase Apoptosis. Assays for apoptosis of caspase apoptosis are well immune cells (such as mast cells).  as mast cells).  assess the ability of polypeptides of the invention (including antibodies and					and Crohn's disease), and pain
Regulation of Caspase Apoptosis. Assays for apoptosis of immune cells (such as mast cells).  as mast cells).  assess the ability of polypeptides of the invention (including antibodies and					management.
caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	HSSJC35	1466	Regulation of	Caspase Apoptosis. Assays for	Preferred embodiments of the
known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and			apoptosis of	caspase apoptosis are well	invention include using
used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and			immune cells (such	known in the art and may be	polypeptides of the invention
			as mast cells).	used or routinely modified to	(or antibodies, agonists, or
				assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of

asthma, allergy,		ıntlammatıon.				<b>t</b>																								
agonists or antagonists of the	invention) to regulate caspase	protease-mediated apoptosis in	immune cells (such as, for	example, in mast cells). Mast	cells are found in connective	and mucosal tissues throughout	the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000); Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor
											_	-																		_
											•																			

et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.		Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For
	IL-2 in Human T- cell 2B9	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1466	1467
	HSSJC35	HSTBJ86
	518	519

1467
HSTBJ86 HSUBW09

	agonists or antagonists of the	nephropathy and/or other
	invention) to activate the FAS	diseases and disorders as
	promoter element in a reporter	described in the "Renal
	construct and to regulate	Disorders" section below),
	transcription of FAS, a key	diabetic neuropathy, nerve
	enzyme for lipogenesis. FAS	disease and nerve damage
	promoter is regulated by many	(e.g., due to diabetic
	transcription factors including	neuropathy), blood vessel
	SREBP. Insulin increases FAS	blockage, heart disease, stroke,
	gene transcription in livers of	impotence (e.g., due to diabetic
	diabetic mice. This	neuropathy or blood vessel
	stimulation of transcription is	blockage), seizures, mental
	also somewhat glucose	confusion, drowsiness,
	dependent. Exemplary assays	nonketotic hyperglycemic-
	that may be used or routinely	hyperosmolar coma,
	modified to test for FAS	cardiovascular disease (e.g.,
	promoter element activity (in	heart disease, atherosclerosis,
	hepatocytes) by polypeptides	microvascular disease,
	of the invention (including	hypertension, stroke, and other
	antibodies and agonists or	diseases and disorders as
	antagonists of the invention)	described in the
	include assays disclosed in	"Cardiovascular Disorders"
	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
	53 (2000); Roder, K., et al.,	described in the "Endocrine
	Eur J Biochem, 260(3):743-51	Disorders" section below),
	(1999); Oskouian B, et al.,	neuropathy, vision impairment
	Biochem J, 317 ( Pt 1):257-65	(e.g., diabetic retinopathy and
	(1996); Berger, et al., Gene	blindness), ulcers and impaired
-	66:1-10 (1988); and, Cullen,	wound healing, and infection
	B., et al., Methods in Enzymol. (e.g., infectious diseases and	(e.g., infectious diseases and

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				carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its	
003	HSUBW09	1468	CD152 in Human T	entirety.	
720		,	cells		
, (	HSVAM10	1469	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
521			IFNgamma using a	a central role in the immune	embodiment of the invention
			T cells	system and is considered to be	includes a method for
				a proinflammatory cytokine.	stimulating the production of
				IFNg promotes TH1 and	IFNg. An alternative highly
				inhibits TH2 differentiation;	preferred embodiment of the
				promotes IgG2a and inhibits	invention includes a method
				IgE secretion; induces	for inhibiting the production of
				macrophage activation; and	IFNg. Highly preferred
				increases MHC expression.	indications include blood
				Assays for immunomodulatory	disorders (e.g., as described
		-		proteins produced by T cells	below under "Immune
				and NK cells that regulate a	Activity", "Blood-Related
-				variety of inflammatory	Disorders", and/or
				activities and inhibit TH2	"Cardiovascular Disorders"),
				helper cell functions are well	and infection (e.g., viral
				known in the art and may be	infections, tuberculosis,
				used or routinely modified to	infections associated with
				assess the ability of	chronic granulomatosus
				polypeptides of the invention	disease and malignant
				(including antibodies and	osteoporosis, and/or as
				agonists or antagonists of the	described below under
				invention) to mediate	"Infectious Disease"). Highly

	imminomodulation regulate	nreferred indications include
		Le cromata marcanoma merado
	inflammatory activities,	autoimmune disease (e.g.,
	modulate TH2 helper cell	rheumatoid arthritis, systemic
	function, and/or mediate	lupus erythematosis, multiple
	humoral or cell-mediated	sclerosis and/or as described
	immunity. Exemplary assays	below), immunodeficiency
	that test for	(e.g., as described below),
	immunomodulatory proteins	boosting a T cell-mediated
	evaluate the production of	immune response, and
	cytokines, such as Interferon	suppressing a T cell-mediated
	gamma (IFNg), and the	immune response. Additional
	activation of T cells. Such	highly preferred indications
	assays that may be used or	include inflammation and
	routinely modified to test	inflammatory disorders.
	immunomodulatory activity of	Additional preferred
	polypeptides of the invention	indications include idiopathic
	(including antibodies and	pulmonary fibrosis. Highly
	agonists or antagonists of the	preferred indications include
	invention) include the assays	neoplastic diseases (e.g.,
	disclosed in Miraglia et al., J	leukemia, lymphoma,
	Biomolecular Screening 4:193-	melanoma, and/or as described
	204 (1999); Rowland et al.,	below under
	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); Gonzalez et al., J Clin	indications include neoplasms
	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
	15:749-795 (1997), and	esophageal, stomach, brain,
	Rheumatology (Oxford)	liver and urinary cancer. Other
when the same of t		

contents of each of which herein incorporated by reference in its entirety.  Human T cells that may be used according to these as may be isolated using techniques disclosed herein otherwise known in the arm Human T cells are primary human I pumphocytes that mature in the thymus and express a T Cell receptor and the cells mediate humoral or of mediated immunity and more preactivated to enhance responsiveness to immunomodulatory factor and transcription of the GATA-3 through GATA-3 signaling pathway in HMC response element in human mast cell line.					38(3):214-20 (1999), the	preferred indications include
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					contents of each of which are	benign dysproliferative
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					herein incorporated by	disorders and pre-neoplastic
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					reference in its entirety.	conditions, such as, for
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					Human T cells that may be	example, hyperplasia,
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in		-			used according to these assays	metaplasia, and/or dysplasia.
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					may be isolated using	Preferred indications include
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					techniques disclosed herein or	anemia, pancytopenia,
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					otherwise known in the art.	leukopenia, thrombocytopenia,
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					Human T cells are primary	Hodgkin's disease, acute
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					human lymphocytes that	lymphocytic anemia (ALL),
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					mature in the thymus and	plasmacytomas, multiple
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					express a T Cell receptor and	myeloma, Burkitt's lymphoma,
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					cells mediate humoral or cell-	disease, inflammatory bowel
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					mediated immunity and may	disease, sepsis, neutropenia,
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					be preactivated to enhance	neutrophilia, psoriasis,
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					responsiveness to	suppression of immune
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in					immunomodulatory factors.	reactions to transplanted
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in						organs and tissues,
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in						hemophilia, hypercoagulation,
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in						diabetes mellitus, endocarditis,
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in						meningitis, Lyme Disease,
HSVAT68 1470 IL-4 in HMC HSVAT68 1470 Activation of transcription through GATA-3 response element in						asthma and allergy.
HSVAT68 1470 Activation of transcription through GATA-3 response element in	522	HSVAT68	1470	IL-4 in HMC		
transcription through GATA-3 response element in		HSVAT68	1470	Activation of	This reporter assay measures	Highly preferred indications
	522			transcription	activation of the GATA-3	include allergy, asthma, and
				through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
				response element in	human mast cell line.	indications include infection
immune cells (such   Activation of GATA-3 in				immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as

as mast cells).	cells has been linked to	described below under
	cytokine and chemokine	"Infectious Disease"), and
	production. Assays for the	inflammation and
	activation of transcription	inflammatory disorders.
	through the GATA3 response	Preferred indications also
	element are well-known in the	include blood disorders (e.g.,
	art and may be used or	as described below under
	routinely modified to assess	"Immune Activity", "Blood-
	the ability of polypeptides of	Related Disorders", and/or
	the invention (including	"Cardiovascular Disorders").
	antibodies and agonists or	Preferred indications include
	antagonists of the invention) to	autoimmune diseases (e.g.,
	regulate GATA3 transcription	rheumatoid arthritis, systemic
	factors and modulate	lupus erythematosis, multiple
	expression of mast cell genes	sclerosis and/or as described
	important for immune response	below) and
	development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
	element that may be used or	diseases (e.g., leukemia,
	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred
	Malm, Methods in Enzymol	indications include benign
	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such

				85:6342-6346 (1988); Flavell	as. for example, hyperplasia.
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
				Quant Biol 64:563-571 (1999);	Preferred indications include
				Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
				J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
18 JF				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
	-			many characteristics of	
				immature mast cells.	
	HSVAT68	1470	IFNg in Human T-		
522			cell 2B9		
	HSVAT68	1470	SEAP in Jurkat/IL4		
522			promoter		
	HSVBU91	1471	Activation of	Assays for the activation of	A highly preferred indication

523	transcription	transcription through the	is obesity and/or complications
	through cAMP	cAMP response element are	associated with obesity.
	response element	well-known in the art and may	Additional highly preferred
	(CRE) in pre-	be used or routinely modified	indications include weight loss
	adipocytes.	to assess the ability of	or alternatively, weight gain.
		polypeptides of the invention	An additional highly preferred
		(including antibodies and	indication is diabetes mellitus.
		agonists or antagonists of the	An additional highly preferred
		invention) to increase cAMP,	indication is a complication
		regulate CREB transcription	associated with diabetes (e.g.,
		factors, and modulate	diabetic retinopathy, diabetic
		expression of genes involved	nephropathy, kidney disease
		in a wide variety of cell	(e.g., renal failure,
		functions. For example, a	nephropathy and/or other
		3T3-L1/CRE reporter assay	diseases and disorders as
		may be used to identify factors	described in the "Renal
		that activate the cAMP	Disorders" section below),
		signaling pathway. CREB	diabetic neuropathy, nerve
		plays a major role in	disease and nerve damage
		adipogenesis, and is involved	(e.g., due to diabetic
		in differentiation into	neuropathy), blood vessel
		adipocytes. CRE contains the	blockage, heart disease, stroke,
		binding sequence for the	impotence (e.g., due to diabetic
		transcription factor CREB	neuropathy or blood vessel
		(CRE binding protein).	blockage), seizures, mental
		Exemplary assays for	confusion, drowsiness,
		transcription through the	nonketotic hyperglycemic-
		cAMP response element that	hyperosmolar coma,
		may be used or routinely	cardiovascular disease (e.g.,
		modified to test cAMP-	heart disease, atherosclerosis,
		response element activity of	microvascular disease,

	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	 invention) include assays	"Cardiovascular Disorders"
	disclosed in Berger et al., Gene	section below), dyslipidemia,
	66:1-10 (1998); Cullen and	endocrine disorders (as
	Malm, Methods in Enzymol	described in the "Endocrine
	216:362-368 (1992); Henthorn	Disorders" section below),
	et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	 85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
	et al., Mol Cell Biol	blindness), ulcers and impaired
	20(3):1008-1020 (2000); and	wound healing, and infection
	Klemm et al., J Biol Chem	(e.g., infectious diseases and
	273:917-923 (1998), the	disorders as described in the
	contents of each of which are	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety. Pre-	urinary tract and skin), carpal
	adipocytes that may be used	tunnel syndrome and
	according to these assays are	Dupuytren's contracture).
	publicly available (e.g.,	Additional highly preferred
	through the ATCC) and/or	indications are complications
	may be routinely generated.	associated with insulin
	Exemplary mouse adipocyte	resistance.
	cells that may be used	
	according to these assays	
	include 3T3-L1 cells. 3T3-L1	
	is an adherent mouse	
	preadipocyte cell line that is a	
	continuous substrain of 3T3	
	fibroblast cells developed	
	through clonal isolation and	

				undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	
523	HSVBU91	1471	Activation of Hepatocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal	A highly preferred embodiment of the invention includes a method for
				transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely	stimulating hepatocyte cell proliferation. An alternative highly preferred embodiment of the invention includes a
				modified to assess the ability of polypeptides of the invention (including antibodies	method for inhibiting hepatocyte cell proliferation. A highly preferred
				and agonists or antagonists of the invention) to promote or	embodiment of the invention includes a method for
				inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be	stimulating hepatocyte cell differentiation. An alternative highly preferred embodiment of the invention includes a
				used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies	method for inhibiting hepatocyte cell differentiation. A highly preferred embodiment of the invention
				and agonists or antagonists of the invention) include the	includes a method for activating hepatocyte cells. An alternative highly preferred
				al., Biol Chem 379(8-9):1101- 1110 (1998); Kyriakis JM,	embodiment of the invention includes a method for
				Biochem Soc Symp 64:29-48 (1999); Chang and Karin,	inhibiting the activation of and/or inactivating hepatocyte

	Nature 410(6824):37-40	cells. Highly preferred
	(2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-	indications include disorders of the liver and/or endocrine
	 500 (1999); the contents of	disorders (e.g., as described
	 each of which are herein	below under "Endocrine
	 incorporated by reference in its	Disorders"). Preferred
	entirety. Rat liver hepatoma	indications include neoplastic
	cells that may be used	diseases (e.g., as described
	 according to these assays are	below under
	 publicly available (e.g.,	"Hyperproliferative
	through the ATCC).	Disorders"), blood disorders
	Exemplary rat liver hepatoma	(e.g., as described below under
	cells that may be used	"Immune Activity",
	according to these assays	"Cardiovascular Disorders",
_	include H4lle cells, which are	and/or "Blood-Related
	known to respond to	Disorders"), immune disorders
· · · · · ·	glucocorticoids, insulin, or	(e.g., as described below under
_	 cAMP derivatives.	"Immune Activity"), neural
		disorders (e.g., as described
		below under "Neural Activity
_		and Neurological Diseases"),
		and infection (e.g., as
		described below under
		"Infectious Disease").
		A highly preferred indication
		is diabetes mellitus. An
		additional highly preferred
		indication is a complication
		associated with diabetes (e.g.,
		diabetic retinopathy, diabetic
		nephropathy, kidney disease

(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	

infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal	tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or	obesity. Additional highly preferred indications include weight loss or alternatively, weight gain.	red in s asso	indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.	Additional highly preferred indications include, hepatitis, jaundice, gallstones, cirrhosis of the liver, degenerative or necrotic liver disease, alcoholic liver diseases, fibrosis, liver regeneration, metabolic disease

					dyslipidemia and chlolesterol
					metabolism.
					Additional highly preferred
					indications include neoplasms
					and cancers, such as,
					hepatocarcinomas, other liver
					cancers, and colon and
					pancreatic cancer. Preferred
					indications also include
					prostate, breast, lung,
					esophageal, stomach, brain,
					and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HSVBU91	1471	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
523				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred
				routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve